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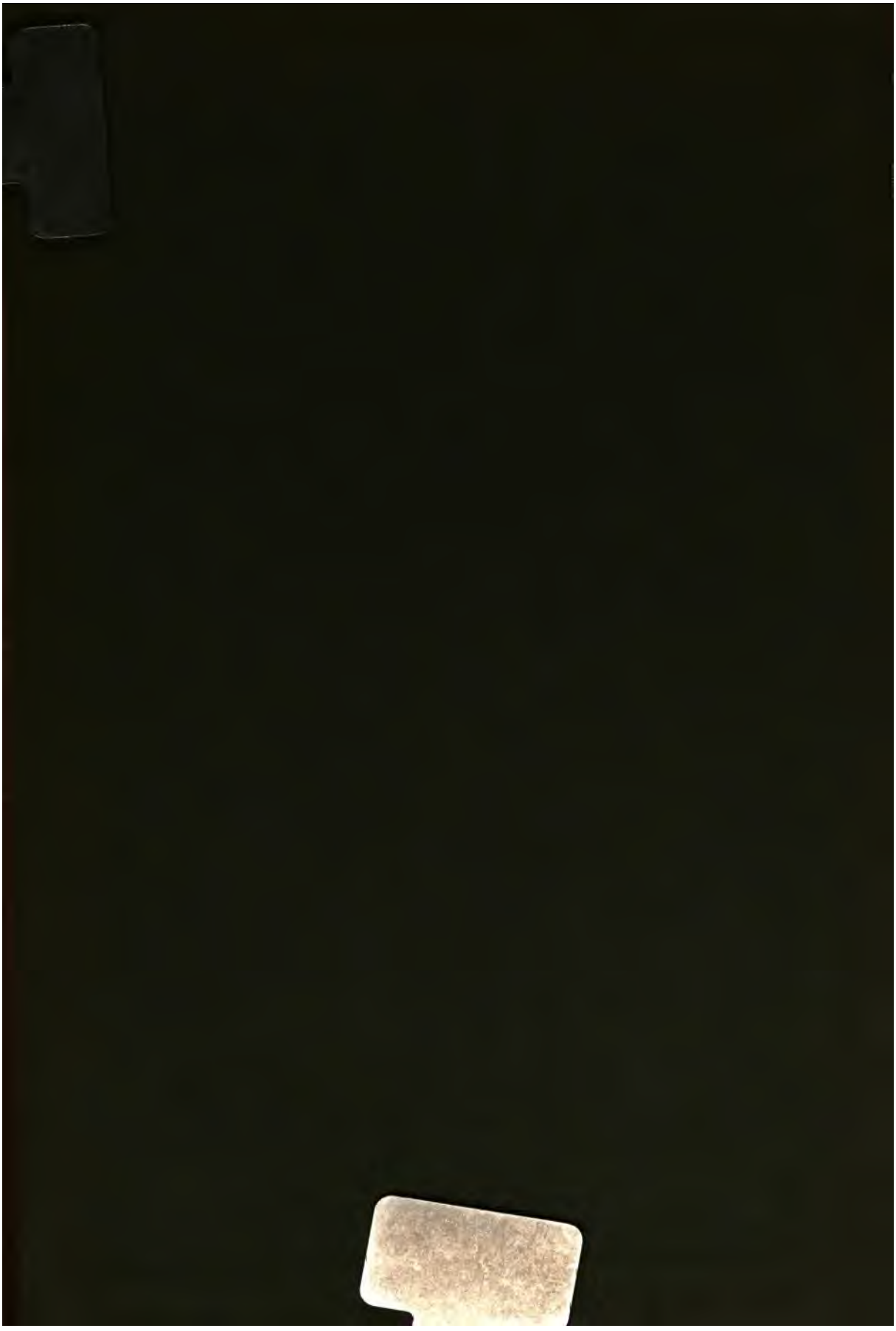

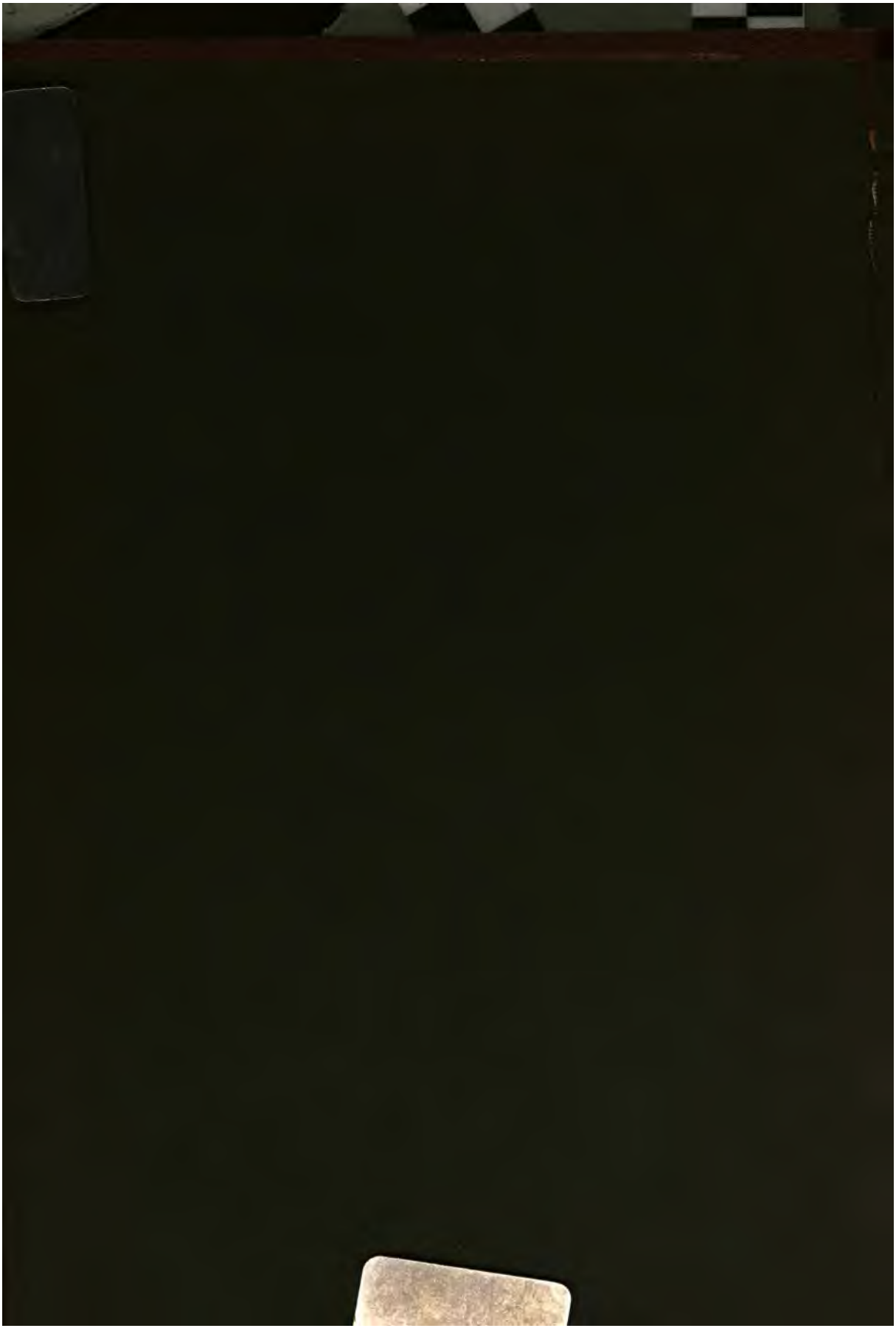

TRANSACTIONS

OF THE

American Therapeutic Society

1911

EDITOR

P. BRYNBERG PORTER, A.M., M.D.

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OFFICERS, 1911-12.

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HARVEY W. WILEY	Washington, D. C.	1910-11

* Deceased.

DECEASED MEMBERS

Samuel Claggett Busey, M.D., LL.D., died Oct. 19, 1899.

William P. Manning, M.D., died Feb. 9, 1901.

John Thomas Winter, M.D., LL.D., died June 22, 1902.

George Edward Tyler, M.D., died July 7, 1902.

Robert Henderson Graham, M.D., died Aug. 24, 1903.

George Bingham Fowler, M.D., died March 6, 1907.

John S. McLain, M.D., died June 2, 1907.

Robert Reyburn, M.D., died March 25, 1909.

Justin Steer, M.D., died June 20, 1909.

Howard H. Barker, M.D., died May 8, 1910.

John Veitch Shoemaker, M.D., died October 11, 1910.

Carl Beck, M.D., died June 8, 1911.

CONSTITUTION AND BY-LAWS.

ARTICLE I.

This Society shall be known as the American Therapeutic Society.

ARTICLE II.

The object of this Society shall be the promotion of therapeutics in its broadest sense.

ARTICLE III.

This Society shall meet annually at such time and place as the Council may determine.

ARTICLE IV.

SECTION 1. The Officers of this Society shall consist of a President, three Vice-Presidents, a Secretary, a Treasurer, and a Council of fifteen members, all to be elected from the active membership, by ballot, at an annual meeting.

SECTION 2. The Council may be convened at any time by the Chairman, at the request of any three of its members. Its decisions shall be equivalent to acts o fthe Society, and shall be reported to it at the next regular meeting. The Council shall elect from its members a Committee on Admissions to consist of three members.

SECTION 3. A vacancy occurring in any office may be filled by the Council.

ARTICLE V.

SECTION 1. This Society shall consist of not more than one hundred active members. Honorary members may be elected on recommendation of the Council.

SECTION 2. Any qualified physician engaged in the general or special practice of medicine or surgery, or in laboratory research of interest in the treatment of disease, is eligible for membership.

SECTION 3. Applications for membership should be made in writing at least one month before the annual meeting. They are to be referred to the Committee on Admissions, which shall, on approval, present their names to the Society at the annual meeting. Five negative ballots shall reject an applicant.

SECTION 4. Applications for membership shall be accompanied by the annual dues for the ensuing year.

SECTION 5. Resignation of members shall not be accepted until all dues have been paid.

ARTICLE VI.

All proposed changes of the Constitution must be offered in writing at a regular meeting. They are to be considered only at an annual meeting, when a two-thirds vote of the members present shall be necessary for their adoption.

BY-LAWS.

1.

The *President* shall preside at the annual meeting of the Society, and deliver an address. He shall appoint a Committee on Scientific Business and a Committee of Arrangements.

In the absence of the President, one of the Vice-Presidents shall preside.

2.

The *Secretary* shall keep a record of the transactions of the Society and of its Committees, conduct all correspondence of the Society, and mail to each member a programme of the meeting, at least two weeks before it is held. The records, publications and seal of the Society shall be in his custody.

The *Treasurer* shall collect all moneys due the Society, disburse the same, as directed by the Council, keep a proper account of all his transactions, and render an annual statement to the Society. He shall have charge of all property belonging to the Society not otherwise provided for.

3.

Ten active members shall constitute a quorum for the transaction of business.

4.

SECTION 1. The *Council* shall constitute a standing committee to consider all matters of interest to the Society. It shall elect a Chairman, Vice-Chairman and a Secretary, and shall appoint an Editor of the Transactions.

SECTION 2. Three members of the *Council* shall be elected annually by the Society, each to serve five years.

SECTION 3. Five members shall constitute a quorum.

5.

The *Committee on Admissions* shall investigate the qualifications of applicants and report at the next annual meeting.

6.

Charges against any member must be made in writing. They shall be referred to the *Council* for investigation.

7.

No papers, report, abstract or other communication, either written or verbal, which, directly or indirectly, commends or advocates any secret, patented or trade-marked product or method of treatment shall be presented to or received by the Society; nor shall any discussion on such product or method be permitted.

Papers are limited to twenty minutes and discussions to five minutes.

8.

The *annual dues* shall be five dollars, payable in advance.

9.

The *order of business meetings* shall be as follows:

1. Reading of Minutes.
2. Reports of Officers and Committees.
3. Election of Members.
4. Presentation of Communications.
5. Miscellaneous Business.
6. Election of Officers.

COMPETITIVE THERAPEUTIC RESEARCH.

On recommendation of the Council of the American Therapeutic Society, at the meeting of the Society held in Boston, Mass., May 14, 1911, it was voted that a prize of two hundred dollars ($200.00) be awarded to the best report on a subject of Therapeutic Research.

1.—The competition is to be limited to members of the Society in good standing.

2.—The subject of the competition is to be limited to a substance or preparation which is official in the United States Pharmacopœia.

3.—The research may be either wholly laboratory or clinical, or laboratory and clinical combined.

4.—The reports must be (a) designated by a distinctive word or motto, and (b) must be accompanied by a sealed envelope marked with the said word or motto, and containing the name and address of the competitor and of the laboratories or hospitals in which the research was conducted. (c) The report and protocol must be typewritten. (d) These must be in the hands of the Chairman of the Committee before April 1, 1912.

5.—The reports and protocols are to be judged by a Committee consisting of the Vice-Presidents of the Society, who shall decide which is the best report as showing valuable therapeutic research, and shall return their decision, together with all the papers submitted to them, to the Chairman of the Council before May 1, 1912.

6.—The Chairman of the Council shall then return the unsuccessful reports to their authors, and shall notify the successful author.

7.—The successful report shall be read by the author on the first day of the meeting, immediately after the President's address.

8.—All matters connected with the competition shall be considered as absolutely confidential by the Chairman of the Council and the Vice-Presidents, except as to the successful competitor.

9.—The Vice-Presidents as judges may divide the prize, or not award it in case no competition is deemed of sufficient merit.

10.—In case any Vice-President shall fail to act, the President of the Society shall be added to the Committee.

Signed: REYNOLD WEBB WILCOX, Chairman.
THOMAS E. SATTERTHWAITE,
SPENCER L. DAWES,

Committee on Prize Competition in Therapeutic Research.

PAPERS READ BEFORE THE SOCIETY.*

ANDERS, J. M.—What Constitutes a Useful Drug, and Shall the Preparations of a Useful Drug be Limited to One or Two? Read by title (1910). (*Monthly Cyclopædia and Medical Bulletin*, Feb., 1911.) Obituary of Dr. J. V. Shoemaker (1911).

BABCOCK, W. W.—The Range of Activity and the Untoward Effects of Certain Spinal Analgesics; Based on Two Thousand Administrations (1910). Uses and Limitations of General Anesthesia as Produced by Subcutaneous and Intravascular Injections. (*Monthly Cyclopædia and Medical Bulletin*, Jan., 1912.)

BARNES, N. P.—Bacterins: their Present Status in Therapeutics (1910).

BARTON, W. M.—Hexamethylenamine in the Treatment of Otitis Media (1910).

BECK, C.—On Morbus Basedowi. Read by title (1910).

BEEBE, S. P.—The Preparation of Thyroid Gland for Use (1910).

BOOS, W. F.—The Newer Heart Remedies (1911).

BROWN, P. K.—A Modified Vaccine Therapy in Pneumonia; with Animal Experiments (1911).

COHEN, S. S.—What Unofficial Drugs are of Sufficient Clinical Value to be Recognized in the United States Pharmacopœia of 1910? Read by title (1910).

CROTHERS, T. D.—The Delusion of the Stimulant and Tonic Effects of Alcohol. (*Monthly Cyclopædia and Medical Bulletin*, July, 1911.)

DA COSTA, J. C., JR.—The Routine Use of the Autogenous Vaccines (Bacterins) in the German Hospital, Philadelphia (1910).

DAVIS, N. S., JR.—Should the Pharmacopœia Contain Only Useful and Efficient Drugs? (*Monthly Cyclopædia and Medical Bulletin*, Feb., 1911.)

FISHER, E. D.—Senile Epilepsy. (*Monthly Cyclopædia and Medical Bulletin*, September, 1910.) General Paresis, Tabes, and Cerebrospinal Syphilis. Read by title. (*Monthly Cyclopædia and Medical Bulletin*, 1912.)

FLICK, L. F.—Skin Inunctions as a Therapeutic Measure. Read by title. (*Monthly Cyclopædia and Medical Bulletin*, August, 1910.)

FUSSELL, M. H.—Further Consideration of the United States Pharmacopœia. Read by title. (*Monthly Cyclopædia and Medical Bulletin*, Mar., 1911.)

GALLANT, A. E.—The Delayed Menopause: its Dangers and Therapeutic Indications. (*New York Medical Journal*, June 18, 1910.) Panhysterocolpectomy for Hernia Vaginæ. (*Monthly Cyclopædia and Medical Bulletin*, Dec., 1911.)

GORDINIER, H. C.—Chronic Acetanilide Poisoning a Perfectly Definite Symptom-complex. (*Monthly Cyclopædia and Medical Bulletin*, 1912.)

GREEN, C. L.—Asthenia Universalis Congenita. (*American Journal of the Medical Sciences*, 1910.)

HUGHES, C. H.—Obituary of Dr. Justin Steer (1911).

KEBLER, L. F.—The Present Status of Drug Addictions in the United States. (*Monthly Cyclopædia and Medical Bulletin*, Jan., 1911.)

---

* For list of papers read before the Society from its organization to the year 1909, inclusive, see the *Transactions* for 1909.

KING, A.—Further Study of Diabetes as an Infectious Disease. (*Monthly Cyclopædia and Medical Bulletin*, July, 1910.) Diabetes Mellitus from a Surgical Standpoint. (*Monthly Cyclopædia and Medical Bulletin*, Aug., 1911.)

KOLIPINSKI, L.—Further Use of Solution of Calcium Creosote in Medicine. (*Monthly Cyclopædia and Medical Bulletin*, August, 1910.) On the Uses of Nickel Sulphate in Medicine. (*Monthly Cyclopædia and Medical Bulletin*, June, 1911.)

LARRABEE, R. C.—The Treatment of Leukemia with the Mixed Toxins of Coley (1911).

LEECH, D. O.—Obituary of Dr. H. H. Barker (1911).

LONG, E. H.—The Metric System. Read by title. (*Monthly Cyclopædia and Medical Bulletin*, Mar., 1911.)

MCPHEDRAN, A.—Treatment of Pneumonia. (*Monthly Cyclopædia and Medical Bulletin*, June, 1910.)

MORGAN, F. P.—Suggestions for the Pharmacopœia of 1910: A Brief Consideration of the Subject in its Relation to the Federal Food and Drugs Act. (*Monthly Cyclopædia and Medical Bulletin*, Mar., 1911.)

MORRIS, R. T.—Surgery of the Obese. Read by title. (*Monthly Cyclopædia and Medical Bulletin*, 1910.) Epithelial Conductors and Obstructors. (*Monthly Cyclopædia and Medical Bulletin*, Aug., 1911.)

MORTON, W. G.—Note on Fluorescence Excited Within Human Tissues as a Method of Treatment. (*Monthly Cyclopædia and Medical Bulletin*, Nov., 1911.)

NAGLE, E. W.—Some Observations on Vaccine Therapy. (*Monthly Cyclopædia and Medical Bulletin*, June, 1911.)

OSBORNE, O. T.—U. S. P., 1910. How May It Be Constructed? (*Monthly Cyclopædia and Medical Bulletin*, Jan., 1911.)

REMINGTON, J. P.—Revision of the United States Pharmacopœia. (*Monthly Cyclopædia and Medical Bulletin*, Feb., 1911.)

ROSS, GEORGE G.—A Case of Recurrent Abscess Formation, Due to Staphylococcus Infection, Successfully Treated by Autogenous Vaccines. Read by title. (*Monthly Cyclopædia and Medical Bulletin*, September, 1910.)

SAJOUS, C. E. DE M.—Acute Hypoadrenia as a Cause of Death, and its Treatment. (*Monthly Cyclopædia and Medical Bulletin*, Dec., 1911.)

SATTERTHWAITE, T. E.—High Frequency Currents in the Treatment of Arteriosclerosis. (*Medical Record*, July 2, 1910.) Malignant Endocarditis in New York City: A Clinical Study. (*Medical Record*, July 15, 1911.)

SHOOK, F. N.—The Malarial Infections and Their Treatment in the Canal Zone. (*Monthly Cyclopædia and Medical Bulletin*, June, 1910.)

SHOUP, J.—Immediate and After Management of the Puerperant. (*Monthly Cyclopædia and Medical Bulletin*, October, 1910.)

SPRIGG, W. M.—Obituary of Dr. H. H. Barker (1911).

STEWART, F. E.—Some Points in Bacterial Therapy. (*Monthly Cyclopædia and Medical Bulletin*, October, 1910.) Dioxydiamidoarsenobenzol as a Patented Product. (*Monthly Cyclopædia and Medical Bulletin*, Sept. and Oct., 1911.)

TAYLOR, J. M.—Some Principles in the Treatment of Chronic Nervous Diseases. Read by title (1910). Remarks on the Treatment of Chronic Disease. (*Monthly Cyclopædia and Medical Bulletin*, 1912.)

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BOSTON MED... OCT ... 1911

SCIENTIFIC PROCEEDINGS.*

TWELFTH ANNUAL MEETING,

Held at the Harvard Medical School, Boston, Mass., May 11, 12 and 13, 1911.

ADDRESS OF WELCOME.

By CLARENCE J. BLAKE, M.D.,
Chairman of the Committee of Arrangements
BOSTON, MASS.

GENTLEMEN OF THE AMERICAN THERAPEUTIC SOCIETY: In the absence of the Dean it is my pleasurable duty to bid you welcome to the buildings of the Harvard Medical School for the holding of your Twelfth Annual Meeting, and I desire to welcome you not only to that which presents itself to the eye, but to the prospective advances which are to grow out of the existing conditions, since here it is proposed to do a manufacturing business of the very highest possible class, in the production of equipped men who are to apply their knowledge, in the broadest sense, to humanity.

These buildings are the product of three distinct and correlative impulses; the impulses offered by the energy and the enthusiasm of members of the medical profession who, some years ago, foresaw the possibility for a new medical school, and proceeded to make the possibility absolute; to those gentlemen we who are here today are indebted for the place in which we hold this meeting, foremost among them that pioneer, J. Collins Warren, and the beloved and revered Henry P. Bowditch, Professor of Physiology. Another impulse toward the erection of these buildings was that which these gentlemen, together with President Eliot, incited in the minds of Mr. Morgan and others, who had, I think, been taught, as more and more of the holders of wealth in this country are being taught by the medical profession, that the very best investment of money, the most productive investment, in behalf of public welfare that can be made is the endowment of scientific research. The third impulse was one which has been growing, in this country especially, within the last twenty years, the appreciation of the fact that the education for so solemn and serious a duty as the care of one's fellow-men should have its basis in connection with the highest educational possibilities of the country, that the

* It is to be understood that the Society does not hold itself responsible for any views expressed by the readers of papers or participants in discussions.

medical school, ceasing to be a proprietary institution or a private venture, should become allied with the university system. Out of these three impulses, incited by members of the medical profession, which placed the medical school distinctly under university control, has come this gift to medical education in which you are today made welcome.

About this group of monumental buildings, which are as adequate in their interior arrangements as they are beautiful in their exterior, you see waste land. The purpose of such waste land so situated is that it should be built upon—it could not be left unproductive—and on this land surrounding the group of buildings of the Harvard Medical School there are to spring up hospitals. The building of the Harvard Dental School is merely a beginning; the Carnegie Research Laboratory, taken as a part of the Harvard Medical School group, is another. There is to be a large children's hospital, and the marble building in process of construction is to be an infants' hospital, of fifty beds. A large hospital for adults will also be a part of the group, since, in later medical education, we have learned that the material as well as the teaching must be under superior control, and one of the arrangements by which these hospitals have been permitted to build upon the land of the Medical School is that which accords to the Corporation of Harvard College the nominating power for the foremost places on each hospital staff.

The relationship between the Harvard Medical School and the hospitals had its beginning in a large tract of land, only a part of which you see is at present occupied. At the instigation of the gentlemen mentioned a tract of land about 26 acres in size was bonded by gentlemen who had money to devote to medical purposes, in sums ranging from $20,000 to $30,000. When the time came for the final donation, of putting up these buildings, these gentlemen, who had offered their money in bonding, presented the site to Harvard University as a gift, and the University was thus able to sell the land at a lower price than would have otherwise been the case.

The Children's Hospital is to have a main building of brick, running along Longwood Avenue, in which there will be an administration center, a large out-patient building, and nurses' home, with a laundry in the rear. The space between that and the Infant's Hospital will be occupied by shacks, in other words, pavilion wards of a comparatively novel form in hospital construction. These shacks will have 2 wards of 10 rooms each, on a ground floor, with a single side room, and the necessary group of administration rooms for each ward; they will be of plaster upon expanded steel and of a special construction which will make it possible to build one pavilion above another without interfering with natural ventilation. The uppermost floor has its sills resting upon uprights extending to the level of the ridge of the monitor roof of the lower pavilion, each pavilion thus having its monitor roof as if it were a single-story building.

One of the problems which has to be worked out beyond the relationship of the hospitals to the medical school is the relation of the hospitals to each other, relationships which would, I believe, be largely furthered and valuably conserved by the establishment of a clearing house for the hospital group.

RESPONSE.

By REYNOLD WEBB WILCOX, M.D.,
NEW YORK CITY, N. Y.

Mr. President, Ladies and Gentlemen, Members of the Therapeutic Society: It is with singular pleasure that the American Therapeutic Society is today the guest of Harvard University. It is more than a formal invitation, and demands more than a formal answer,—it is a coming home, for amongst the members of the American Therapeutic Society there are some that are coming home today, a good many of us who are coming back to the Harvard Medical School. Many of us, and I am one of them, recall those old days when we sat in that dilapidated old building in North Grove Street, the odors from the dissecting room in the west end of which could be detected at least from Cambridge Street.

We have seen the Harvard Medical School going to Boylston Street and the Dental School taking our old quarters. We of the older generation remember the Harvard Medical School in brick, and we see it now in marble. We have seen the days when the medical student was not taken care of and no attention was paid to his comfort, and we now find him a pampered guest of a great university.

Eleven years ago the Therapeutic Society was started in Washington; it was during a period of therapeutic nihilism. The Therapeutic Society started an awakening. We have come from our very humble beginnings as Harvard came, and now we are occupying a distinguished scientific pre-eminence and are fittingly received as guests in a scientific palace. Two years ago we were recipients of a magnificent entertainment by Yale, and now we expect great things of Harvard. Another year, and we pass across the border and shall be guests of the great university there; just across the imaginary line which the legislators from many of our States are trying to break down. The fame of McGill knows no limit, political or otherwise.

We appreciate the honor which Harvard has extended to us, and we hope that the intellectual stimulus which we receive at Harvard will be turned back again to her in the better care that we all may be enabled to give to those patients whom it may fall to our lot to treat. In this way Harvard may receive advantage from our meeting under these most favorable auspices.

OBITUARIES.*

DR. JUSTIN STEER.

By C. H. HUGHES, M.D.,
ST. LOUIS, MO.

Dr. Justin Steer, who died at the age of 63 in his St. Louis home June 20, 1909, was an honored and worthy member of this society, an upright, patriotic citizen, beloved by many friends and a large clientele of patients. He was enthusiastic, devoted, and painstaking in the pursuit of the scientifically therapeutic side of his profession and a well-informed and successful clinician who knew well how to efficiently apply his therapeutic resources.

He held numerous positions of honor in his profession, but the highest of all was the esteem in which he was held in the hearts of his fellow practitioners of his favorite art and vocation.

With his estimable family, we mourn his untimely loss to them, to his professional patrons, and to us, an aggregated body, seeking to promote the welfare of mankind through rational and efficient therapeutic discovery and through right remedial endeavor.

DR. HOWARD HINES BARKER.

By D. OLIN LEECH, M.D.,
AND
WILLIAM M. SPRIGG, M.D.,
WASHINGTON, D. C.

Hardly had our last session closed when death claimed one of our members. Howard Hines Barker, M.D., LL.D., one of the charter members of this Society, and its President 1903-4, was called to his reward May 8, 1910, at 2.45 A.M., at his home, in the city of his birth, Washington, D. C.

His education was obtained at Union Academy, Everett Institute, and Columbian College. He was graduated in medicine from the Medical Department of Georgetown University in 1870. The degree of LL.D. was conferred on him by the National University in 1890.

Dr. Barker was a physician of more than average ability, but was modest and retiring in his nature, almost to the point of diffidence. He was a great lover of home, family, and friends. He was a man of rare good sense and excellent judgment, one whose counsel was sought by younger men in the profession, whose friendship and advice, when once given, could be counted upon in time of need. He was greatly beloved by his many patients, who showed their sorrow at his funeral. The funeral service of Dr. Barker was held at his home, Wednesday, May 11th; it was simple, but impressive. The rooms were taxed to their capacity by his many associates, friends, and patients. The

* Read at the Twelfth Annual Meeting of the American Therapeutic Society.

floral tributes were profuse and beautiful, silent testimony of the love and sorrow of those to whom he ministered in life.

Dr. Barker was born in Washington, D. C., Sept. 13, 1848. In 1872 he married Miss Fannie Rozelle Wilson, of Washington, D. C., who with one son, Howard Wilson Barker, survive him. After his graduation in medicine, he entered Columbia Hospital for Women, and became Resident Physician in 1871. It was here that he showed preference for that branch of his profession, obstetrics, in which he excelled. He was Demonstrator of Anatomy for two years and Lecturer on Anatomy for one year at his Alma Mater.

He was a founder of the Central Dispensary and Emergency Hospital, where for many years he was in charge of the department of diseases of women. He was Consulting Physician to the Eastern Dispensary and Casualty Hospital. He was a founder, in 1884, of the Medical Department of the National University, was its Dean and Professor of Obstetrics and Gynecology up to the time of its merging with George Washington University. He was a founder of the Washington Obstetrical and Gynecological Society, a founder and Ex-President of the Therapeutic Society, D. C., a member of the old Clinico-Pathological Society, a member of the Medical Society of the District of Columbia and the Medical Association of the District, and its President in 1904. He was also a member of the American Medical Association. He was deeply interested in, and untiring in his efforts toward, the advancement of his chosen profession.

The following resolutions were presented and adopted by the Society:—

WHEREAS, God in His wise providence has removed from our midst our late associate, Dr. Howard Hines Barker, therefore be it

Resolved, That this Society deeply deplores the sudden taking off of our esteemed associate, and expresses its deep regret at the loss of so valuable a man to the Medical Profession and the community at large.

Resolved, That this Society enter upon its minutes this testimonial of esteem, and that a copy thereof be forwarded to his family.

DR. JOHN V. SHOEMAKER.

BY JAMES M. ANDERS, M.D., LL.D.,
PHILADELPHIA, PA.

JOHN VEITCH SHOEMAKER was born at Chambersburg, Pa., March 18, 1852. The family history is interesting, since not a few ancestors were prominent in Central Pennsylvania from colonial days until the present. The subject of this sketch was the oldest son of Lewis A. Shoemaker, who was born at Chambersburg, and married Miss Mary M. Greenawalt, also a native of that town. Dr. Shoemaker's paternal grandfather, Anthony Shoemaker, came to America from Prussia about the middle of the eighteenth century; he settled at Chambersburg, Pa., and here he afterward married a Miss Michael, who had been born near Edinburgh, Scotland. It is probable that Dr. Shoemaker

inherited a strain of that canny Scotch shrewdness which is proverbially attributed to the race of Bruce and Wallace. Among his antecedents were several who played important rôles during the War of the Revolution.

After spending his boyhood days at the paternal home in Chambersburg, he entered Dickinson College, Carlisle, Pa., taking both the preparatory and academic courses and graduating with honors (receiving the bachelor's degree) in 1872. In the autumn of the same year he matriculated at the Jefferson Medical College, Philadelphia, from which institution he received the degree of Doctor of Medicine in 1874. After graduation he was immediately appointed a demonstrator of anatomy, and he also organized the "Jefferson Quiz Association," and soon could boast of the largest quiz class in the College, his subject being Materia Medica and Therapeutics. In 1875 he opened a dispensary for the treatment of diseases of the skin. This venture having proved highly successful, the Jefferson Hospital was compelled to provide accommodations for patients suffering from this class of affections, and he was appointed Lecturer on Diseases of the Skin at Jefferson Medical College in 1883. In 1876 he was made Lecturer on Diseases of the Skin at the Philadelphia School of Anatomy.

Having gained an enviable reputation in Diseases of the Skin, he was in 1886 called to the chair of Dermatology and Genito-Urinary Diseases at the Medico-Chirurgical College. It was to the growth and upbuilding of this institution that Dr. Shoemaker subsequently gave a large measure of his talents, zeal, and constructive energy. Chiefly through his efforts, funds were obtained for the erection of the new Medico-Chirurgical Hospital, which he also served faithfully as visiting physician, trustee, and treasurer. Three years later he was requested to accept the chair of Materia Medica, Pharmacology, and Therapeutics in the same college. This chair he held until the time of his death, and his lectures were throughout brilliantly successful and popular. As showing the important rôle played by Dr. Shoemaker in the remarkable development of this institution, I may be allowed to quote the words of a colleague, to be found elsewhere: "It is difficult, in contemplating the career of this remarkable man, to do him adequate justice for the work he has performed for the Medico-Chirurgical College and Hospital. For twenty-four years he has labored for it not because he felt that, as a member of its faculty, it was his duty to do so, but because for him there is only one institution, one hospital, and one love—the Medico-Chirurgical College."[1]

Dr. Shoemaker's literary work is extensive and varied, both in periodicals and books. In the midst of his multiform professional duties Dr. Shoemaker found time to write the following popular and well-known books: "A Practical Treatise on Diseases of the Skin," "Poisons and their Antidotes," "Heredity, Health, and Beauty," and "Materia Medica, Pharmacology, and Therapeutics." Upon these works largely rested Dr. Shoemaker's high standing as an author and practitioner, as well as his wide reputation as an expert witness, in which

[1] T. H. Weisenburg, M.D., "The Medico-Chirurgical College and Hospital," Founders' Week Memorial Volume, Philadelphia, 1909, page 327.

capacity he was constantly requested to serve in many notable trials, both in Philadelphia and elsewhere. He was one of the founders in 1879 of the *Medical Bulletin,* which after the first year he conducted alone. In 1887 Dr. Shoemaker instituted the *Medical Register,* which he afterward merged with the *Medical Times,* under the joint title *Medical Times and Register,* a medical journal that has enjoyed wide repute.

A complete list of his writings which are extant would occupy more space than the limits of this sketch would permit. Of the many articles from his pen, the most important probably was that on the "Oleates," which he read before the British Medical Association, at Belfast, in 1884. The novelty and therapeutic importance of these preparations—an untrodden field—were clearly presented in this paper and attracted much professional attention both abroad and at home. Another essay of signal value was that on "The Treatment of Diseases of the Skin by Novel Means and Methods"; this he read in the same year as the American Representative of the American Medical Association, before the International Medical Congress at Copenhagen, Denmark.

Dr. Shoemaker held membership, both active and honorary, in many local and national societies. He was successively secretary, vice-president, and president of the American Medical Editors' Association. He was a member of the American Medical Association and trustee from 1890 to 1893; a member of the American Academy of Medicine, Philadelphia County Medical Society, the Medical Society of the State of Pennsylvania, the Mississippi Valley Medical Association, the Minnesota and New Jersey Medical Societies, Association of Military Surgeons of the United States, British Medical Association, and a fellow of the London Medical Society, and president of the American Therapeutic Society in 1908. Dr. Shoemaker was secretary of the committee of the American Medical Association that had charge of the arrangements for the Ninth International Medical Congress at Washington, in 1887; also a delegate to the Tenth International Medical Congress at Berlin in 1890, to the Pan-American Medical Congress at Washington in 1893, and the Eleventh International Medical Congress at Rome in 1894. In the same year (1894) the degree of LL.D. was conferred on Dr. Shoemaker by Dickinson College, Carlisle, Pennsylvania.

Dr. Shoemaker had a laudable desire to become a figure in public life. He quietly went on making friends among those occupying prominent official positions in city and State, while engaged in an extensive office and consultation practice, in teaching and other responsible duties, and, as it were, waiting his chance. It came after his heroic and successful services in behalf of the Government during the Spanish-American War. Soon after the beginning of hostilities between this country and Spain, in 1898, he organized a staff of surgeons and nurses, and at a public meeting of physicians and citizens in the Medico-Chirurgical Hospital, April 22, 1898, he offered their services to the U. S. Government. At the request of General J. P. S. Gobin, who appealed to Dr. Shoemaker in August of that year to send a relief train for the sick soldiers at Camp Alger, Dr. Shoemaker raised the necessary funds, and on August 24, 1898, presented to the State of Pennsylvania its first well-equipped hospital

train, which the Adjutant-General, Thomas J. Stewart, conducted to Camp Alger. The task undertaken by him in this connection was a comprehensive one, yet it was speedily carried out with marked success. Dr. Shoemaker has been justly lauded for the high efficiency and patriotism which he manifested during that conflict. During the months of August and September of the same year more than 500 sick and wounded soldiers were brought to the Medico-Chirurgical Hospital from the fever-stricken camps and about as many to the other hospitals of Philadelphia, under the direction of General Stewart. It was a direct outcome of this work, and it was in recognition of its vast importance, that Governor William A. Stone, on January 30, 1899, appointed Dr. Shoemaker Surgeon-General of the National Guard of Pennsylvania, a position which he held during four years, and to which he devoted a vast amount of time and labor, effecting a more complete organization of the Medical Department.

In 1901 the then Mayor of Philadelphia, Samuel H. Ashbridge, appointed Dr. Shoemaker President of the Board of Charities and Correction, and here his organizing abilities promptly manifested themselves in various radical changes in matters pertaining to municipal health and hygiene. Among notable improvements, special mention should be made of plans for a general hospital quite apart from the City Insane Asylum and the City Almshouse.

In 1908 Mayor Reyburn, of Philadelphia, appointed Dr. Shoemaker a member of the Committee on Founders' Week. He was subsequently made chairman of a committee on Scientific Institutions, Medical Colleges, and Hospitals. This committee not only organized and exhibited a fine museum in the City Hall during Founders' Week, but likewise held a large representative meeting of the profession, with public exercises, in the Walnut Street Theater, November 9, 1908. Under his guidance this same committee published a permanent volume of twelve hundred pages, well illustrated, upon all the scientific institutions, medical colleges, and hospitals of Philadelphia from the foundation of the city.

Dr. Shoemaker had undeniable qualifications for tasks involving organization, while his capacity for executing work was truly enormous. He seemed to be peculiarly fitted by birth, mental endowments, and a fine presence to initiate schemes having for their object the improvement of the public service, more particularly municipal institutions and sanitation, and, by injecting his personality, to carry them into effect. His bearing was cordial and attractive, and his kindly nature won him many friends and patrons by whom he was much beloved. As a teacher his sympathetic nature and cordiality of manner placed him naturally in the most pleasant and harmonious relations with the student-body. Dr. Shoemaker had among his troops of patients many persons of great prominence both in public and private life. He had a social disposition, which made him a welcome guest at banquets, receptions, and on less formal occasions among his friends, both lay and medical. Dr. Shoemaker never failed to drop a kind and cheering word to all with whom he came in contact—rich or poor. He was of average height, and his features were finely cut, regular, and quite attractive.

Dr. Shoemaker died October 11, 1910, after an illness lasting about two years, of chronic nephritis, at the comparatively early age of 58 years. His, however, was a life of great usefulness not only as a medical practitioner and teacher, but also when considered from the viewpoint of the public service. It is fair to assume that had Dr. Shoemaker not shown so great devotion to his professional labors during the many months in which his health was slowly declining, but manifested more obedience to the earnest counsel of his physicians, his life might have been considerably prolonged. He was laid to rest in his native home, Chambersburg, Pennsylvania.

PRESIDENT'S ADDRESS: BROMATOTHERAPY.

By H. W. WILEY, M.D.,
WASHINGTON, D. C.

It has long been recognized in investigations in the field of preventive medicine that food is one of the most valuable agents for combating infection and warding off sickness. The well-nourished man is, to a certain extent, immune from ordinary infections and diseases. It is not my purpose today to enter into a discussion of the theories relating to immunity in a well-nourished organism, save to call attention to the fact that in such an organism all the functions of the body are so harmoniously arranged as to present an undivided front to any common enemy. The presence throughout the body of organisms capable of attacking and destroying undesirable germs is well known. It is generally regarded that precautions taken by the public in the control of their food supply are health measures. In fact, this is regarded as a fundamental basis for the making of pure-food laws by the States and by the nation.

In some quarters an erroneous idea prevails concerning this important fact, viz., that there is no necessity for regulating traffic in foods unless it can be shown in individual cases that specific foods produce well-marked injurious effects. This view is entirely too narrow to cover the scope of such legislation. It is advisable to keep well to the fore, as a guiding principle, the idea that the health of a community depends largely on the character and quantity of the nutrients which it consumes.

Fasting Increases Susceptibility.

The experiments which have been made in regard to the susceptibility to various diseases during fasting and starvation afford another illustration of the truth of the proposition. The fasting or starving animal is much more subject to the action of deleterious or poisonous substances than the animal which is in a proper state of nutrition. This fact will receive further attention. Even in specific cases it is well understood that the administration of a deleterious drug has its effect somewhat softened by being combined with an abundance of nutritious foods. The general principle that pure, nutritious foods are prophylactic and tend to preserve the health of the community is uncontested. The question may be asked how this can be reconciled with advice which is frequently given by physicians to abstain from foods for a certain time for specific reasons. I think a brief inquiry will show that it is only an apparent contradiction of the general statement which has been made above. The advice to fast or diminish the quantity of food ingested is only given in cases where it is evident that either an excess of food has been habitually consumed or that the organs of digestion have become so debilitated from some cause as to be unable properly to handle the usual amounts of food.

In such cases total or partial rest from the ordinary functions will do more good to the patient than the apparent danger of fasting, or partial starvation, will do harm. When one has eaten too much at any given meal or during a given period of time, it is a well-known fact that fasting or partial abstinence from food will in a short time produce a most beneficial effect, easily recognized by the patient himself. It would be a dangerous proposition, it seems to me, to change the ordinary number of meals. In other words, the general idea of three meals a day is, in my opinion, not incompatible with the proper rest of the digestive organs, while, on the other hand, it is advisable from the point of good and sufficient nutrition. Of course, it is quite impracticable to lay down any general principle on this point. It has been stated recently as a result of experimental determination that more than the customary three meals a day results not in the consumption of more, but of less, food. Granting that this may be the case, it does not follow that the increasing of meals beyond the usual number of three would give any beneficial results. The constant feeding even in a small way would undoubtedly interfere with the normal conduct of the digestive function, which is in its essence a periodic one and not a continuous performance. The separation of the usual three meals a day over a wider period might be advantageous and is worthy of consideration. The ordinary professional man usually crowds all three of his meals into a very short period, say between 8 o'clock in the morning and 8 o'clock in the evening, leaving a period of rest of twelve hours between the last meal at night and the first one in the morning. Perhaps a somewhat earlier breakfast, and possibly a later evening meal, increasing the period covered by the three meals to fourteen hours, would be an improvement. This, however, is hardly a matter for discussion at the present time.

Food as a Remedy.

Leaving with these introductory words the value of food as a prophylactic, let us come to the essence of the problem and see if we can ascertain the functions of food as a remedy. It is interesting to trace the history of the functions of food in disease in the various phases of changing opinion among medical men. For instance, we will take the old adage, "feed a cold and starve a fever," as being a concrete expression of crass ignorance of the remedial value of food. Perhaps if the treatment were reversed it would not be so contrary to the truth. Upon the whole, I may say the general principle of medical practice today is opposed to the idea of starvation as a remedial measure. In practically all disease there is an increased catabolism, while, as a rule, there is a diminished anabolism. The predominant condition of disease, in other words, is waste. Naturally there are exceptions to this rule, as in the case of obesity, where just the opposite condition prevails. A moment's consideration of the common diseases of mankind shows how almost universally the principle of waste is a dominant factor. In fact, the progress of the disease, or the rapidity of the healing process, is measured, as a rule, by the loss or gain of weight. It is perfectly evident that if a man in a normal condition of health, and of practical equilibrium of body weight, begins to lose flesh without any apparent cause it

is a grave symptom to be carefully considered. It is true that a man who is preparing for a prizefight or an athletic contest does reduce his weight purposely, either by restriction in his food or by increasing the vigor of his exercise, but a man at his ordinary vocation, following the usual mode of life, and eating his normal food who finds himself losing weight must become suspicious even though he may be unable to locate the disorder. Very often, in fact in most cases, this acceleration of catabolism or retardation of anabolism is accompanied by an increased temperature due, of course, to the more rapid destruction of tissue, and thus fever has also come to be regarded as one of the characteristic symptoms of most diseases. It must be admitted that the man who some time during the day experiences a rise of temperature, even though it be slight, should regard that as a grave symptom of disorder and disease. Of course, I do not refer to slight variations in the body temperature which are periodic and due to natural causes, but to those cases in which no assigned cause can be given.

It follows from this that one of the first and most continuous duties of the physician is to seek in some way to repair the waste, and, if he can, control directly the accelerated catabolism and improve the retarded anabolism. Since derangement of the digestive organs and loss of appetite are such common symptoms in disease, even when the digestive organs are not directly affected, one of the first duties of the physician is to recommend a ration which may tend to stay the ravages of the disease and restore the normal weight and character of the tissues. I think I may be permitted to say without criticism and without any animadversion that the study of the problem of nutrition in disease, so important in therapeutics, has not received the attention it deserves in the medical colleges of our country. The case may be stated in this way, viz., that the average physician of the United States, and perhaps of the world, is not as well prepared as he should be to handle the problem of the nutrition of his patient in a scientific, systematic, and effective manner. It is true that, as in other departments of medicine, the science of nutrition is to a certain extent empirical. In deranged appetite it is almost useless to crowd the stomach with food which the patient abhors. Unless something can be secured which appeals to the taste it is difficult to get a proper digestion and assimilation of the food product. The digestive organs are, moreover, often so disturbed and so sensitive to irritation that the most nutritious food products produce general discomfort, nausea, and vomiting, or, if retained, diarrhea with its kindred ills. Nevertheless, out of the mass of evidence there are slowly crystallizing certain general principles of bromatotherapy which are taking such form as to justify statement, arrangement, and discussion.

Empirical Character of Our Knowledge.

The principal difficulty which is encountered in discussing a problem of this kind on a strictly scientific basis is the empirical element in our knowledge. While the general effects of the administration of foods are well understood, the specific ways in which these foods act, either as a preventive or remedy in

disease, are not wholly understood. The studies of metabolism in the past have been almost exclusively devoted to the digestibility, absorption, and excretion of the principal elements of food, namely, nitrogen, sulphur, and phosphorus. The energizing portions of the food, as distinguished from the tissue-building portions, have only of late years been subjected to scientific investigations. It was not until the perfection of the respiration calorimeter by Atwater and his associates that we were able to get accurate scientific data respecting the energy elements of foods.

Prof. Francis G. Benedict[1] says: "In order to bring preventive medicine to the present successful stage, innumerable experiments, involving microscopy, chemistry, and physiology, were necessary to demonstrate in just what manner these baneful organisms (for in many instances they have proved to be organisms) enter into our bodies and produce diseases. . . . Pasteur, Lord Lister, and Koch are household names today and stand for wonderful series of painstaking researches which have developed the fact that many diseases formerly thought inevitable in the course of a lifetime can, by reasonable care, in a large number of cases be avoided. . . . It is my privilege to explain to you how it is hoped to develop another line which, while it has by no means the attractive outlook presented by bacteriology and preventive medicine in general, may yet prove to be of the greatest value to mankind. I refer to investigations in the nutrition of man. If by proper study we can find what foods are best adapted to different purposes, if in what quantities they should best be ingested, what preliminary treatment is most desirable, we will have solved a great many problems regarding diseases of digestion and will have made a large contribution to a wider branch of preventive medicine."

The method of exact study which is afforded by an apparatus of this kind, enabling the experimenter to determine the actual degree of heat produced, and bringing under control the metabolism and the expired gases of the pulmonary mechanism, opens up a field of the widest significance and value for further investigations. One more striking example may perhaps be cited in which the respiration calorimeter was used to determine the quantity of energy consumed in ridding the body of an added ingredient, namely, borax. Dr. Rubner[2] studied the effect of the consumption of energy, where the food remained constant, on two individuals, the only change being in the administration of a small quantity of borax in each case. He found that the consumption of energy during the boron period in both cases was increased; very much more in one case than in the other, the increase in the one instance amounting to 21.7 per cent. and in the other 5.3 per cent. It is highly significant that in this instance not only was injury shown to be produced in other ways, but especially in regard to the deflection of the energy from its normal purpose to the work of ridding the body of a foreign substance. This is not a factor which is to be neglected in the consideration of food as a

[1] Proceedings of the American Philosophical Society, July, 1910, vol. xlix, pp. 145 and following.

[2] Arbeiten aus dem Kaiserlichen Gesundheitsamte, Neunzehnter Band, mit 3 Tafeln, 1902, pp. 70-88.

therapeutic agent. It is evident that the full value of the food should be secured, especially since in nearly all cases of illness the digestive powers are impaired. The danger of placing on the system at that time the additional burden of ridding the body of an agent such as a chemical preservative is evident. A striking example is thus afforded by the calorimeter of the threatened danger to health implied by the deflection of so large an amount of the natural energy which should be secured from the food to a totally unnecessary and foreign purpose, namely, the elimination of an added product which imposes a burden of very great magnitude upon the system.

Protein Consumption.

It is evident that a final determination of the question now so widely agitated, viz., the relative quantity of protein which should be contained in the diet, can only be definitely answered by investigations in which an actual determination of the energy produced in the body can be made under varying conditions. It does not seem at all likely that man in the process of his evolution should have acquired a dietary habit which is of such a character as to constantly threaten his efficiency and his health, as is believed by those who claim that the necessary content of protein in our diet is probably only about half that which the human animal has naturally chosen. The respiration calorimeter will permit of an exact study being made of the energy developed by varying quantities of food, although it cannot in its very nature answer that very important question as to the effect upon the human organism in many years, or even generations, of a half protein diet. The virtues of a low protein diet have been set forth very fully by several authors, and the discussion of this question has already been so interesting, as well as complete, that there is nothing which I could add here save a general observation that such a radical departure from the established dietary of man might *a priori* be regarded as prejudicial to the best development of the human animal. To establish the continued efficacy of a low protein diet would require very prolonged observations before any final conclusions as to its permanent benefits could be formed. At the same time it must not be forgotten that increasing knowledge based on wise and conservative experimental data may show that man has not chosen entirely wisely in his selection of the best possible diet for his physical wellbeing. Before any dogmatic statements can be made respecting the so-called excess of protein in our food we need more scientific data in regard to its utilization than we have at the present time, while it would be necessary to wait perhaps a century or more to see what the general effect of the protein diet cut in half would have upon the human race.

Specific Protective Nature of Foods.

I have called attention above to the general principle that is now well recognized by competent authorities to the effect that good, nutritious, and wholesome foods exert a general protective influence against infection. It is of interest to refer here to the further elucidation of this problem by the

studies of Dr. Reid Hunt,[3] on the poisonous effects of the nitriles on small animals. The nitriles are supposed to owe their poisonous effect to the development of hydrocyanic acid as a result of their decomposition in the system. Hydrocyanic acid is recognized as one of the most virulent and rapidly acting poisons. The inhibiting effects of various agents were studied in connection with the activity of the nitriles given to mice. A remarkable difference in tolerance of the poison was shown under different diets. The resistance of the animals was varied in the most marked degree by changes of diet.

Dr. Hunt summarizes the results of his investigations as follows[4]:—

1. A restricted diet markedly increases the resistance of certain animals to acetonitrile.

2. Guinea-pigs upon a limited diet excrete a smaller percentage of the cyanogen of acetonitrile as sulphocyanate than do those upon an unrestricted diet. This result is interpreted as showing that certain specific processes of metabolism are retarded in partial inanition.

3. Diet has a marked effect upon the resistance of animals to certain poisons; the resistance of some animals may be increased fortyfold by changes in diet.

4. Certain diets, notably dextrose, oatmeal, liver, and kidney, greatly increase the resistance of mice to acetonitrile; their effect is similar in this respect to the administration of thyroid.

5. The effect of an oatmeal diet in increasing the resistance of certain animals to acetonitrile is probably due in part to a specific effect of the diet upon the thyroid gland; this is an illustration of how an internal secretion may be modified in a definite manner by diet.

6. Diet has, in certain cases, a marked effect upon the reaction of animals to iodine compounds; this effect is probably exerted largely through the thyroid. The condition of the latter is more important than the chemical form in which the iodine is administered.

7. Certain diets (notably eggs, milk, cheese, and various fats) greatly lower the resistance of certain animals to acetonitrile; their effect is the opposite of that of thyroid.

8. Several glands (notably prostate, ovaries, and testes) have an effect upon the resistance of animals to poisons similar to, but much less marked than, that of thyroid. Other glands (thymus, parathyroid, suprarenals) have either no effect or an effect opposite to that of thyroid.

9. The resistance of animals to propionitrile is markedly influenced by diet.

10. Diet causes distinct but not very marked differences in the resistance to morphine.

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[3] "The Effects of a Restricted Diet and of Various Diets upon the Resistance of Animals to Certain Poisons"; Hygienic Laboratory Bulletin No. 69, June, 1910.

[4] *Loc. cit.*, pp. 88-89.

11. Season has an important effect upon the resistance of animals to certain poisons; in some cases these effects seem to depend upon seasonable variations in the activity of the thyroid.

12. The experiments show that foods such as enter largely into the daily diet of man have most pronounced effects upon the resistance of animals to several poisons; they produce changes in metabolism which are not readily detectable by methods ordinarily used in metabolism studies. The ease and rapidity with which certain changes in functions are caused by diet are in striking contrast with the essentially negative results obtained by the chemical analyses of animals fed upon different diets.

The above investigation establishes beyond doubt the value of diet in influencing the attitude of the body to certain administered poisons, and it is fair to infer that a similar change would also be effected in the resisting powers of the body to the usual causes of disease.

Food as a Cause of Disease.

That foods may be a direct cause of disease in certain conditions is a well-known fact. One of the most familiar illustrations of this fact is scurvy, a disease which is due principally to the continued and exclusive use of cured foods, especially meats. The disease is removed only when the cause of its production ceases to exist and fresh vegetables and fruits form at least a part of the dietary.

Another mysterious disease which has long puzzled medical men is beriberi, which occurs principally in rice-eating countries. Extensive investigations made as to the cause of this disease have indicated that it was seen in its greatest virulence among soldiers, and especially sailors, confined almost exclusively to a diet of rice. In other words, beriberi apparently holds the same relations to rice as scurvy holds to cured meats. One of the most interesting of the modern developments with respect to beriberi is the fact that it is now believed to be caused but rarely by natural rice, but rather by rice which has been polished. Polishing rice is a process whereby its outer coat is largely removed, and together with it the layer of phosphate cells found immediately beneath the external covering. Japan has succeeded in stamping out beriberi from her navy by an improved dietary, while in Java the Dutch physicians have reported that a mixture of other foods with rice has vastly reduced the prevalence of this disease. Further than this, the Dutch physicians found that when rice was eaten unhulled, that is, unpolished, the proportion of cases among the soldiers was only 1 in 10,000, while, on the other hand, if the outer covering was entirely removed the proportion was 1 to 39. It is evident from this that one method of preventing the introduction of beriberi into this country, where the consumption of rice is largely increasing, would be to forbid the importation of rice which has been polished or treated in a similar manner, and to forbid interstate commerce in such rice as having undergone a treatment which may render it injurious to health.

The latest contribution to this subject is that of Dr. Victor G. Heiser,

Director of Health of the Philippine Islands, who has summarized the evidence which has been collected in a recent article entitled "Practical Experiences with Beriberi and Unpolished Rice in the Philippines."[5]

Dr. Heiser gives some interesting data showing the relation between polished rice and beriberi in the Culion Leper Colony. Beriberi was a very prevalent disease in this colony until February, 1910, when the use of unpolished rice was made compulsory. The total number of deaths at Culion from February, 1909, to February, 1910, was 898, and of this number 309 were due to beriberi. From February, 1910, the time the use of unpolished rice was made compulsory, to February, 1911, the total number of deaths, in a population greater than that of the previous year, was 369. Of this number only 2 deaths were due to beriberi. This suggested that a good treatment for beriberi would be the material removed from the rice by polishing. At the end of January, 1910, 50 patients in the Culion Leper Hospital undergoing treatment for beriberi were given 15 grams of rice polishings twice daily. Two patients who were in a very advanced stage of the disease died on this treatment, but all of the others began at once to improve. Within two weeks half of the number were able to leave the hospital, and in four weeks every patient with beriberi was reported as cured. Prior to May 10, 1910, beriberi was very common throughout the Philippines. In May, 1910, an executive order was issued by the Governor-General of the Philippine Islands prohibiting the use of polished rice in all public civil institutions. Since August, 1910, only 2 cases of beriberi have arisen in these public institutions, one of which was among the crew of the steamer "Rizal," and an inspection of the ship's stores showed that the crew's rice was of the polished variety. Dr. Heiser concludes his summary as follows:—

"On account of the successful experience with unpolished rice in the prophylaxis of beriberi in the Philippines during the year, and since these data confirm the work of Fraser, Stanton, Aron, Kilbourne, De Haan, and Highet, as reported at the last annual meeting of the Far Eastern Association of Tropical Medicine, it is believed that the time has come for the medical profession to aid in completing the last step in the test which promises to place another weapon in the hands of prophylactic medicine for the eradication of another of the world's serious and costly diseases."

Buttner opposes the idea, which is quite prevalent, that beriberi is a disease which is at least favored, if not caused, by a low protein diet, by stating that modern medical opinion, as voiced by Henri Salanone,[6] is to the effect that the old theory in regard to the cause of beriberi is rapidly giving way, and that the disease is due to a specific infection. Granting for the sake of the argument that this may be true, it appears that this specific infection only attacks those who have been subjected for a long time to a low protein diet, such as that afforded by rice.

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[5] The Journal of the American Medical Association, April 29, 1911, vol. lvi, No. 17, pp. 1237-38.

[6] Bulletin de la Société de Biologie, June 30, 1908.

Effect of Idiosyncrasy.

Many wholesome foods are said to produce disease in specific instances, due undoubtedly not to the nature of the food, but to individual idiosyncrasy. The eruption which occurs in some persons after eating strawberries is an illustration of this. Other persons who are idiosyncratic have a peculiar aversion to some forms of wholesome food, *e.g.*, potatoes, while some are unable to eat soups or other things to which flavors have been added. In these cases the source of the trouble is not to be sought in the food itself, but in the peculiar constitution of the individual. Undoubtedly the continued consumption of certain forms of food must produce a profound impression upon the organism; hence the necessity for insisting upon a wholesome, well-balanced diet for healthy individuals. For a similar reason the conservative mind will look with some suspicion upon recommendations for radical changes in normal diets, although such changes may apparently be attended for a time with favorable results. Based on this general principle, it is easy to infer that *a priori* it is a safe thing to reject all the various theories of abnormal diets which are continuously being presented. The exclusive consumption of nuts or fruits or uncooked foods, vegetables or meats, or preserved foods, has nothing from a theoretical point of view to commend it to the favorable consideration of the consuming public. Radical changes also in the balanced ration, unless to produce some specific, well-understood effect, are *a priori* to be rejected. We can understand why a man at hard labor should have an increased quantity of carbohydrates or fats, and for the same reason we can understand that when plumpness is desired the comparative quantity of carbohydrates and fats may be increased, or *vice versâ*. The character of the diet undoubtedly influences both the physical and mental condition of the people who consume it over centuries of time. If the people of New England had eaten for three hundred years the pork and corn bread of the laborer instead of the fish, bread, bean, and pie diet actually consumed, we doubtless would have found Harvard University a quite different institution.

Food a Carrier of Typhoid.

An interesting account of an outbreak of typhoid fever in London in the autumn of 1910 is reported in the *British Medical Journal* of March 18, 1911, p. 638. The attention of Dr. Hamer, a medical officer of health, was directed to an outbreak of typhoid fever of about 300 cases. After a careful examination he came to the conclusion that at least two-thirds of the 300 cases must have been due to some special cause, and a search was made for it. Of the 200 patients examined in clusters or groups of infection, all but 5 or 6 belonged to the poorest classes of the population. From the stage of the disease it was concluded that most of the infection must have occurred from the 10th to the 12th of August. In a large majority of the cases the history of the diet at that time included fried fish. Naturally the frying could not have had anything to do with the typhoid outbreak, except by lack of its completeness. The area of this infection contained numerous "fried-

fish houses." The fried fish is a cheap article of diet, being made chiefly from what is called "late" fish—in other words, the fish belated in its arrival to market or left over from the sale—and these "late fish" fall largely into the hands of the small friers. The inspection of such fish is, unfortunately, not very thorough, and the author states that there is no systematic control by a sanitary authority, such as is now required in the case of other sources of food.

Decay of Teeth.

Attention is called to the opinion of dentists that the early decay of teeth which prevails among the present generation is due to the excess of soft starchy food and sugar in the diet of people, especially children.[7] Bread containing a certain proportion of bran requires more mastication and would act as a natural cleanser of the teeth. When the people of England ate coarser bread and their food was rougher their teeth were better. Many remedies for the correction of the evil have been proposed.

Allusion should be made to the "no breakfast plan," and the "fasting cure," the great apostle of which was the late Dr. E. H. Dewey, who had an inadequate medical education in the University of Detroit fifty years ago, and a checkered experience as surgeon in the United States army during the Civil War. The great discovery attributed to Dewey was that the people in America ate more than was good for them, and that many of their troubles could be relieved by partial or total abstinence. His plan was, to begin with, the allowance of only two meals a day, breakfast being omitted; but afterward, emboldened by his theories, he prescribed prolonged fasts, and had many followers. One of his disciples, a Mr. Carrington, published a book in which he contended that food is not a source of energy and heat, but Dr. Dewey himself, in his work entitled "No Breakfast Plan and the Fasting Cure," published in 1900, does not commit himself so clearly. He recognizes that in the United States the gospel of three square meals a day has received a most complete acceptance.

Foods Used as Drugs.

Under the Food and Drugs Act the same substance may at one time be classed as a food and at another as a drug. As an illustration of this may be cited olive oil, which not only is a standard food, but is also included in the Pharmacopœia as a drug. There is, however, a large class of modified foods which are advertised for the use of invalids, and as such would have to conform to the standards prescribed for drugs, and be labeled in harmony with the requirements of the law. These foods include that large class of so-called meat extracts and preparations in a soluble form, and modified foods such as gluten flour and gluten bread, etc., specifically intended for some special disease, and to which attention has already been called.

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[7] British Medical Journal, No. 2563, Feb. 12 and 19, 1910.

The value of medicinal foods must be estimated (1) from the amount of nutriment which they contain, and (2) from their availability in case of disordered digestion. Unfortunately, in most diseases, even those which do not specifically affect the digestive organs, the digestive functions are seriously deranged, and in this condition the ordinary foods are not properly digested and assimilated. It has been in the hope of remedying this defect in the function of digestion that so many therapeutists and physicians have endeavored to modify ordinary foods in such a way as to make them more suitable and useful in case of disease.

The number of these modified foods is legion, but the number which are of specific value is limited. The preparation of meat extracts on a large scale is becoming a business of considerable magnitude, and it would not be in harmony with the facts to say that such preparations are without value. When made from fresh, wholesome meat, and under sanitary conditions, it is difficult to say in what respect they are inferior to the home-made article. It seems, however, to be an unfortunate fact that foods which have been prepared for a long time, even without undergoing changes which are perceptible by ordinary chemical or bacteriological observation, do not appear to have the same nutritive value as those which are freshly prepared. Where it is possible, therefore, it is advisable that meat extracts intended for invalids should be prepared at home, or at least immediately before consumption. It would not be proper here to enter into the various methods of preparing these meat extracts, but these methods can be obtained from the therapeutist, the physician, or standard works on the subject. Unfortunately, the amount of nutriment in meat juices is extremely small, and for this reason the Council on Pharmacy and Chemistry of the American Medical Association has made a special study thereof. In the opinion of the Council the so-called invalids' foods, or predigested foods for invalids' use, should be equally as nutritious, volume for volume, as good, wholesale milk, and doubtless one-fourth of this nutritive value should be of a nitrogenous character. It should be remembered that to sustain the strength and body weight of the patient during a serious illness, and to prevent a degree of waste which threatens death, not less than two quarts of milk, having a food value of 1400 calories, are required per day. If the ordinary medicinal preparations, such as meat juice, are to be depended upon for this amount of nourishment, it is seen at once that enormous volumes of them must be administered. These quantities would tend to keep the digestion of the patient in a disordered condition, threatening intoxication, even if the quantity of the material could be tolerated. It is difficult to see, therefore, under what circumstances any better food may be secured than that prepared from pure, wholesome milk, with such modifications of the fresh milk as may render it as suitable as possible to the wants of the patient. Analyses of large numbers of so-called invalids' foods have shown that some of them contain less than one-sixth the nutrient power of milk, while the best of them, as a rule, have no greater nourishing power than milk itself. In addition to this, it must not be forgotten that many of these so-called foods contain, for preservative

purposes, alcohol or glycerol, neither one of which can be regarded as a safe substance for administration in many forms of disordered digestion. From a therapeutic point of view the value of the preparations of invalids' foods may be taken under serious consideration as to their effect and composition. It is to be realized that in hospitals, and where patients are in indigent circumstances, it is difficult to procure fresh, wholesome milk, fresh meat juices, or other fresh foods which an invalid might possibly tolerate, and in these cases, of course, reliance must be had upon the next best thing, namely, the best and most wholesome of the prepared articles.

The addition of gelatin to meat extracts to increase their nitrogenous content has been largely practised, and this practice must be looked upon with some suspicion by the therapeutist and physician. Protein, for instance, contains compounds such as tyrosin and tryptophane, which are not found in gelatin. Further than this, it is believed that gelatin alone, even in a state of health, would not support life for any considerable period of time, while the true proteins will do so. The use, therefore, of extracts and meat preparations containing gelatin is to be deplored, since such preparations do not have the composition, and hence not the value, of true extracts of meat, although their nitrogenous content may be largely increased.

Infant Foods.

Much experimenting has been done and many articles written in the last few years on infants' food. Many manufacturers are preparing and placing on the market foods for the use of infants in which they claim, with some insistence, that they are imitating as nearly as possible the natural food which the infant should have. As with most other subjects connected with nutrition, there are many differences of opinion respecting the virtues of prepared foods for infants. The manufacturers, a few of the consumers, and a still fewer number of physicians believe they have merit and urge their general use. The great majority of the medical profession, however, looks with suspicion upon such prepared foods, especially as there is no means of knowing how long they have been prepared, to what bacterial or other infection they may have been subjected, and what the attitude of the infant's digestive fluids would be toward them. The differences become more pronounced in cases of the disease of the digestive tract which is peculiarly an infantile disease and which prevails especially in hot weather.

Experience has borne out the general idea current among physicians that where it can possibly be obtained the only substitute for normal mothers' milk for infants is the milk of other animals, modified to resemble as nearly as possible the composition of mothers' milk. The difficulty, in the first place, of securing a pure milk for modification, and, in the second place, of having it modified in a proper manner without danger of deterioration, makes the problem of the feeding of infants deprived of their natural food one of most serious consequence. Here is a case where the slightest error of judgment or of administration threatens not only the health, but the actual life, of the child. The great mortality among infants is made possible largely by

digestive disturbances due to improper food. It seems to be a perfectly plain proposition to state that if the sick infants of this country could have a digestible and normal food the percentage of recovery would be enormously increased. The therapeutic value of foods is more pronounced in the case of infants than in any other case we could consider. Without meaning to cast any suspicion upon a wholesome diet for infants other than a milk diet, I am constrained to say that such diets should never be used except as a last resort when a proper milk diet is unobtainable.

My own experience in modifying milk may be of some value, based, as it is, upon the method employed in the Westminster Hospital for Infants in London. The great mortality among infants led the managers of the hospital to try to secure a commercial article of milk which was pure, clean, and fresh. Having failed in this, the authorities determined to establish their own dairy, which they did, with healthy cows in the country, at a convenient distance from London. The fresh milk from this dairy could be delivered at the hospital for consumption in a few hours after being drawn from the cow. Based on the general principles followed in this case, I had a series of experiments carried out showing the possibility of securing a modified milk, suitable for all ages of infant life and also suitable for use in diseased conditions, and delivering it for consumption within a few hours after milking. The milk of healthy cows was placed in a separator while still warm and converted into cream and skimmed milk. All the apparatus and vessels used were sterilized, and immediately after separation the cream and milk were cooled to 40° F., placed in double-walled milk cans with an intervening air space, and delivered to the railway. In two hours the milk was in the laboratory, where it was modified by being separated into certain standard solutions. First the cream was reduced with sterilized skimmed milk to the content of 20 per cent. butter-fat, and stored at ice temperature; the skimmed milk was of constant composition, being taken from the same cows, so that an occasional analysis was all that was necessary to be certain of its exact content of protein, milk-sugar, etc., and it was also kept at ice temperature; a standard solution of lime-water was made with sterilized water, and kept at ice temperature; a standard solution of milk-sugar was made with sterilized water and likewise kept at ice temperature, and sterilized, cold, distilled water was kept constantly on tap. With these standard solutions it was possible, by mere volumetric measurement, to produce immediately any milk product desired for which previous chemical standards had been set. Such standard milks were made according to the age of the infants to be fed, and were delivered to the Children's Hospital within four hours after the milk had been drawn from the udder.

The ease and celerity with which such pure standard milks can be prepared can only be realized when once their preparation has been undertaken and successfully completed. My experience leads me to the belief that there would be no difficulty whatever in supplying every city in the United States with pure, clean, modified milk, suitable for infants' use, at a cost very little above that of ordinary high-grade milk. Physicians and hygienists through-

out the country should work to secure the adoption of such a standard, and municipalities should enact laws forbidding the feeding of infants with artificial foods other than those which are standardized and kept pure and wholesome. The grown-up people may continue to consume an ordinary, clean milk with perhaps little danger, but such milk cannot be used for infants without great danger.

I should like to say just a word in passing on the very important subject of pasteurization. In my opinion pasteurization of milk for infant feeding should not be practised. At best, pasteurization is a choice between two evils, since it is not necessary except in the case of bad or improperly handled milk. The only excuse for pasteurization is the danger of infection by pathogenic germs. I do not see how pasteurization in any way affects the filth question; it can only be useful by its action on pathogenic germs, but milk containing pathogenic germs should not be permitted to be sold. Hence, pasteurization is advisable only when the character of the milk is unknown and when it is likely to be contaminated. This does not warrant its use for infants in any circumstances except those of necessity. The universal adoption of pasteurization would give a false security which, to my mind, would tend to delay the era of pure milk. On the other hand, I cannot praise too highly the philanthropic motives of those who believe in pasteurization and have given their time and their money to make it effective. We must confess that the general milk conditions of cities are so bad that pasteurization appears to be about the only way to secure immediate alleviation. An effort should be made to secure so clean a milk that pasteurization would no longer be necessary. There is great danger, too, in milk being represented as pasteurized when, in point of fact, it is not so, and investigations have convinced me that much of the pasteurized milk is in about as bad a condition bacteriologically as that which has received no treatment at all.

The modification of milk by the introduction of other bodies such as starch, cereal broths, etc., has also received very considerable discussion. As a rule, the consensus of medical opinion is against the practice, although many physicians believe in it and prescribe certain additions of cereals or cereal products to foods for infants, especially those of several months of age. One of the latest contributions to the literature on this subject is that of Dr. Giffhorn,[8] who states that "from the beginning of the fourth month milk which has been mixed with certain gruels or soup may be given without danger." He also contends that "the former general opinion that the use of gruels or soups diminished the resistance of the child to disease and promoted atrophy, rickets, scrofula, etc., is a mistaken one." Nevertheless, he admits that "the excessive use of soups without milk will, if continued for a long time, lead to the most severe injury, which has been described as 'flour nutrition disease.' This disease is indicated by an arrested and diminished weight, leading to extreme thinness, and a peculiar condition of the muscles, so that passive movements are executed with greater difficulty.

[8] Fortschritte der Medizin, p. 176, Feb. 23, 1911.

Edema also follows such exclusive use of cereal foods." With this admission on the part of the author, it can hardly be deemed advisable to mix such foods with milk when milk, as is well known, forms a complete nourishment for children, not only under 4 months of age, but for a long time thereafter.

It has also been claimed by some in the last few months that the mechanical modification of milk by passing it under tremendous pressure through small orifices—a practice commonly known as homogenizing—renders it more suitable as a food for infants. It is certain that this process does disturb the fat globules, and so distributes and fixes them in the mass of milk as to render it difficult for the cream to rise and be separated. If the size of the fat particle affects the digestibility of the milk, as may be reasonably supposed, some benefit may be derived from this mechanical treatment. Since the treatment is wholly mechanical, no objection can be made to it in so far as percentage constituents of the body are concerned. Whether homogenizing be used for fraudulent purposes or not is another matter. I am speaking only of its use on milk and cream for the purpose above mentioned.

A most important contribution to the subject of infant-feeding in cases of bacillary dysentery has been made by Dr. Arthur I. Kendall, of the Department of Preventive Medicine and Hygiene, Harvard Medical School. Based on the observation that the bacilli which are causative in infantile dysentery have their activities very profoundly modified by the environment in which they grow, Dr. Kendall undertook to modify this environment in the intestinal tract of the infant by means of the food administered. The theory of the modification rests upon a fact which has been well established, viz., that these organisms which produce poisonous bodies by their activity in an environment of protein produce harmless bodies in an environment containing certain forms of carbohydrates. Simple acids which are formed by the activity of these organisms upon carbohydrates are harmless, or comparatively harmless, and the presence of the carbohydrate protects the protein bodies largely from the ravages of bacterial action. Inasmuch as the products of bacterial activity are often toxins, and thus favor the production of autointoxication, the prevention of such activity must undoubtedly prove of therapeutic value. Dr. Kendall suggests the most promising of carbohydrates for this purpose, namely, milk-sugar, which is the natural sugar of the normal food of the healthy infant. Pronounced benefits were secured by the use of this food product in cases of infantile dysentery caused by bacilli. Attention is called, of course, to the fact that milk-sugar alone is not a sufficient food for infants, but it may be administered with great benefit for several days after the preliminary cleaning of the bowels by the usual methods, and the best results are obtained when it is administered at frequent intervals. The prevention of the formation of poisonous matters in these cases is of the highest therapeutic importance. After the danger period has passed, the gradual return to food containing protein can be safely accomplished.[9]

[9] Details of these investigations may be found in the Boston Medical and Surgical Journal, No. 9, pp. 288-294, March 2, 1911, and in the Journal of Medical Research for April, 1911.

Sour-milk Treatment.

Much has been said in the last few years respecting sour milk as a preventive and remedy for disease, and as a means of prolonging life. Most persons who have become enthusiasts in this line attribute the theories of healing to Professor Metchnikoff. It is true that Metchnikoff has written much on the subject of sour milk as a food, but a careful perusal of his work does not afford any reasonable foundation for the sentiments which have been attributed to him. The effect of sour milk upon the intestinal flora is a matter of scientific, and doubtless hygienic, importance, and from the extent to which the study of this interesting problem has been carried as a result of Metchnikoff's writings the latter have certainly been productive of good. Even if sour milk should appear from the results of present investigations to prolong life, too short a time, as yet, has elapsed for its observation to permit of making any dogmatic statement of this kind. The fact that people who consume large quantities of sour milk live to a ripe old age is of no consequence, since a great many who do not make their diet on sour milk also live for a long period. It would be necessary to carry on comparative experiments, beginning with infants and continuing through childhood, middle life, and old age, to determine with any certainty the value of this theory. Naturally such an experiment would have to be prolonged through sixty to eighty years to have a true scientific basis.

As a result of the sour-milk theories the country is flooded with advertisements of cultures of different kinds to be used for the artificial souring of milk. These cultures are accompanied with most extravagant statements respecting the virtues of this diet, intended to deceive and mislead, and too often succeeding in the purpose for which they are published. It is the duty of those interested in therapeutics to study, without bias, the data relating to all claims of this kind, but to be slow in reaching conclusions, especially in attributing virtues to certain diets which are not fully proved by proper scientific and experimental evidence.

In this connection I may say that probably too much stress is laid upon the dangers of intestinal bacterial action by most writers of today. One would almost think from a perusal of some of the literature that the existence of bacteria in the intestines is a matter of regret. We cannot, however, accept such a theory in view of the fact that doubtless since the beginning of man the intestinal flora has flourished and multiplied in numbers beyond the comprehension of man. To such an extent is bacterial life developed in the intestines that it is asserted by some authors that a very considerable portion of the total weight of fecal matter is composed of bacteria.

The field is, of course, a large one from the therapeutic point of view, and a study of the changes which take place in the bacterial flora of the intestines under different forms of diet would bring to light much valuable information. Antiseptics might be introduced also into different parts of the intestinal canal by enclosure in media which would require different times for their digestion, so that the antiseptic would be set free at stated

intervals during the passage of these bodies through the alimentary canal. In this connection a more extended study of the chemical composition of the feces under varying forms of diet would be a necessary concomitant of the bacterial study.

Alcohol as a Remedial Agent.

A bitter controversy has been raised over the question, "Is alcohol a food?" Again the respiration calorimeter has come to our assistance in this matter, and it has been shown by Atwater and his assistants, at Middletown, Conn., that the average adult human organism is able to oxidize with practical completeness a considerable quantity of alcohol per day. This quantity, of course, varies in different individuals, but may be placed fairly accurately at about 3 ounces of alcohol per day for each person. This quantity must be distributed over different periods of the day, as to take it all at once would not only defeat the purpose of the experiment, but in most cases probably produce actual intoxication.

I think there is a marked tendency in the medical profession to regard the virtues of alcohol as very questionable. The old idea that if one is about to expose himself to extreme danger or extremes of climatic conditions the body should be fortified by the use of alcohol has disappeared. It is quite certain now that the taking of alcohol does not make one any less apt to freeze, but more so, and that it does not yield any such quantity of energy as to be at all compensatory for the injury it may otherwise produce. I have stated on the witness stand, in answer to a question, that I considered alcohol to be a food because a certain quantity of it is burned in the body and results in the production of heat and energy. In the light of the investigations which have been made, and from theoretical conditions, I am inclined to the opinion that the effort to rid the body of alcohol, even in the relatively small quantities I have mentioned, perhaps consumes a great deal more energy than is furnished by its combustion, and that upon the whole alcohol cannot be regarded as a food even in the limited sense above specified. It is without question a substance which does not nourish the body, build tissue, or repair waste, and it is quite likely that its value either as a food or medicine has been greatly overestimated.

In an article in the *Popular Science Monthly*,[10] Prof. Graham Lusk has summarized in an interesting way the available literature on this question under the title "Alcohol—its Use and Abuse." The action of the German Emperor in calling attention to the abuses incident to the consumption of alcohol has led to a wider discussion of this problem in many circles, and the effect of alcohol upon the children of Bavaria in particular has been cited as an instance of its harmful properties, especially when offered to and consumed by those of tender years. The German Emperor now permits his health to be drunk in a glass of water, and this, it is claimed, will be a great stimulus toward the restriction of alcohol-drinking in the German army.

The susceptibility of alcohol addicts to certain diseases has been noted by many writers. Apparently, persons using alcohol, especially if it is taken

[10] Popular Science Monthly, April, 1911, vol. lxxviii, p. 381.

constantly or in some excess, are more sensitive to solar radiation than those of abstemious habits. The records of death by sunstroke indicate that a very large percentage of those who suffer from insolation are addicted to the use of alcohol. Dr. Reid Hunt, in the paper already referred to on the effect of nitriles on small animals, found that mice which had previously been given alcohol were much more susceptible to poisonous influences than those which had not. The tendency which alcohol undoubtedly has to weaken the bodily resistance is not a matter to be left out of consideration.

The general result of the study of this problem has been an accelerated movement to restrict or limit the use of alcohol in medical practice, and especially in hospitals. A few years ago the administration of some alcoholic beverage was regarded as necessary in the treatment and elimination of the causes of disease. At the present time the use of alcohol in any form as a food or drug product is extremely restricted. The idea that alcohol stimulates mental effort and produces facility of expression is rapidly disappearing. It is doubtful whether a single brilliant thought or poetic or elegant expression has ever owed its origin to alcohol in any form. It is true that alcohol seems to take the bridle off the tongue and give free rein to conversation, but this effect is produced by a paralyzing influence on the sense of responsibility, rather than a stimulating influence upon the general flow of ideas. Alcohol undoubtedly relieves the individual under its influence from his sense of responsibility as a moral agent and permits a freer expression of ideas, even if they are not so good as those which would be expressed with greater reluctance in the normal state. Both as a means of prevention of disease and as a remedy for disease, alcohol is rapidly falling into disrepute and bids fair to become a mere memory in the materia medica and in the Pharmacopœia.

The agency of alcohol as a cause of insanity has been recognized by most authors, but all are not agreed upon this question; the same is true regarding cirrhosis of the liver, which by many writers is attributed largely to the consumption of alcoholic beverages. That alcoholism in parents influences unfavorably the mentality, morality, and physical being of the offspring seems to be a well-recognized fact. The question may therefore suggest itself whether there is any further necessity for the use of alcohol except for technical purposes. In this summary, of course, I have not taken into consideration the social feature of alcoholism, nor that other feature which it is important to keep in mind, viz., the danger of removing from human observation and experience forces which make for the bad. If this could be accomplished throughout the whole realm of human relations, there might result an environment wholly favorable to the production in the near future of an individual who, without the struggle and temptation which his ancestors had endured, would lack all the fine attributes of man, as well as his vices.

Vegetables vs. Mixed Diets.

Many different opinions are expressed by competent observers in respect to the merits of a strictly vegetable and a mixed diet. In the *New York Medical Journal* of January 14, 1911, the editor, speaking of the book of Dr.

J. L. Buttner, states that he has made a good case for exclusive vegetarianism on the part of convalescents, patients preparing for surgical operations, and the victims of gout, rheumatism, and skin diseases. Doubt is expressed whether the taste for meat is an acquired one. On the contrary, it seems to be innate. Attention is called to the experience of the poet Tennyson, who tried to subsist on an exclusively vegetable diet for a short time, but was compelled to desist, as he found his vigor, both mental and physical, deserting him. "As regards meat," the editor says, "there can be no doubt of its bacteria-carrying properties, or of the strain it throws upon the organs of digestion and elimination, particularly of individuals who do little physical work out of doors."

On the other side, it may be well to call attention to a fact which the editor of the *New York Medical Journal* seems to have forgotten, namely, that vegetable foods are also carriers of bacteria, as well as animal foods—even more so—and that the strain on the digestive organs in the assimilation and excretion of vegetable foods is as great as if not much greater than is the case with animal foods. The true superiority of the vegetable diet is not found in the fact that it is more easily digested or imposes a smaller burden on the eliminating organs, but rather in the fact that as a rule it is a more complete ration, carrying with it in many cases all the elements necessary for nutritive purposes. For this reason, if we were compelled to make a choice between an exclusive vegetable diet and an exclusive meat diet, there would be no hesitation on the part of any well-informed person in regard to the preference which should be made.

In this connection attention may also be called to the fourth edition of "A Cook Book for Nurses" which has just been issued by Sarah C. Hill. Nurses are presumably charged with the care of the sick and convalescent, as well as of infants, and this practical nurse by no means favors an exclusive vegetable diet. In fact, milk takes the first place in the "Fluid Diet," followed by broth, beef-juice and beef-tea; while tea, coffee and cocoa are placed before fruit beverages, barley and rice waters, and toast. Gruels and milk soups also form an important part of the dietary. Under the "Light Soft Diet" are broths and soups with grains, eggs, cereals, ice-creams and ices. A "Soft or Convalescent Diet" begins with sweetbreads, calves' brains, fish, chicken, squabs, and eggs—all these coming before potatoes, asparagus, peas, cauliflower, fruits and desserts. This is not mentioned as an authoritative expression of opinion, but only to show what a trained nurse has been taught to consider a proper diet.

The work of Dr. J. L. Buttner, entitled "A Fleshless Diet," appeared in September, 1910. In this work Dr. Buttner has brought together the usual arguments in favor of a vegetable diet, but he has failed to show any scientific basis for the conclusions which he draws. He devotes a whole page, for instance, to showing that meat is an unwholesome and dangerous food, and that in certain cases persons who are vegetarians have exhibited great strength and endurance, quoting the observation on a low protein diet with approbation. In all of these matters he comes very wide of a truly scientific discussion of the

subject. On page 9, under "Vegetarianism and Disease," Dr. Buttner discusses particularly matters pertaining to bromatotherapy. He says:—

> In truth, the highest duty of the physician is to teach the means to preserve health, but in his profession he meets continually with people who, for whatever cause, have developed sickness which it is no more in his power to prevent. Diet at that time is a therapeutic measure of the highest importance. The value of a proper dietetic management in disease is realized more and more. The best diet that can be devised for any given patient is not always of equal importance, but it is a factor which should never be lost sight of. To help recovery it may be the primary and most important, or it may be of secondary value, provided the dietetic habits of the patient are not too bad. We must remember also that in disease, still more than in health, diet must be suited to each individual, and no sudden or sweeping modification can be made without due regard to what was before, however desirable it would seem to make a radical change, for even most injurious habits must be handled with care.

With the above statements of cardinal principles, I most heartily agree. Dr. Buttner goes on to suggest a purely vegetable diet for all forms of disease, but modifies his advice in the following manner:—

> Therefore, though in the following pages we indicate an absolute fleshless diet for many diseases, we would not think it advisable to impose it suddenly and without careful consideration.

He quotes with approbation from the paper of Dr. Victor Pauchet, presented at the Congress of Surgery, Paris, 1909. Dr. Pauchet speaks particularly of the preparation of the patient for a surgical operation. He states:—

> To obtain these results it is necessary to *nourish* the patient up to the last moment, that is, up to six hours before the operation. Thus his resistance is not diminished. It is necessary *to wash* the liver, the kidneys, and the tissues with a certain quantity of liquid, neither too great, not to tire the heart and kidneys, nor too small, as the elimination of the toxins of the body must be complete before the operation. It is necessary to give foods which, besides being devoid of toxins, should at the same time be a bad culture medium for intestinal germs. These conditions are fulfilled by a vegetable or especially a fruit *régime*.

That fruit juices are wholesome and nutritious no one will deny, and a proper adjustment of the diet preparatory to a capital or even a minor operation will be approved by every surgeon. But many, perhaps, would choose a mixed rather than a purely vegetable diet.

Diet in Diabetes.

One of the most striking illustrations of the value of food as a therapeutic agent is undoubtedly presented by that very prevalent disease, diabetes mellitus. The works on medicine are full of formulæ for controlling the food supply in this condition of disordered metabolism. The principal effort in the control of the food supply in these cases has been to restrict to the smallest possible extent those portions of the diet which are easily converted into dextrose. Although it is claimed that other varieties of sugar are sometimes found in the urine, the principal and usually the only sugar therein found is dextrose. Since the inversion of cane-sugar produces one-half of its total weight of

dextrose, and inasmuch as the conversion of starch results practically in changing all of it into dextrose, these two substances have been particularly singled out as those which should be controlled in diabetic patients. Naturally the thought suggests itself here that by this method we are treating only a symptom, and not the disease; and a further consideration must not be lost sight of, viz., that by the abnormal change of the diet which would be brought about by excluding sugar and starch entirely the other organs of the body might be so affected that more injury than good would result. Still, it is a cardinal principle in the treatment of diabetes to diminish the output of sugar as rapidly as possible, since it is believed that in doing this the foundations are laid for recovery, or at least for improvement in the disordered conditions which have produced this symptom. It is evident at once that the principal disturbance in metabolism which leads to the excretion of sugar in the urine is a failure to burn the carbohydrates completely in the body. It is, of course, still a question, why a selective combustion of carbohydrates should take place, such sugars as levulose being practically completely oxidized, while the dextrose remains unacted upon. This assumption, however, may be fallacious.

The dahlia bulb contains, instead of starch, inulin, which upon hydrolysis yields levulose. It might be inferred from this that the dahlia bulb would be an acceptable substitute for starch for diabetic patients, just as levulose has been used instead of dextrose in such cases. Formerly it was understood that the levulose was oxidized; later researches have led to the belief that it is transformed in the blood and tissues to dextrose and is eliminated in the latter form by diabetics. Hence the use of the dahlia root instead of starch, or of levulose instead of sugar, would probably not yield the benefits expected.

I will not burden this paper with any accounts of the modifications of the diet for diabetics further than to say that the choice of food poor in starch and sugar lies at the foundation of practically all dietaries for this purpose. Inasmuch, however, as the entire exclusion of starch from an article like bread would render it unpalatable, and, in view, further, of the difficulty of securing a starch-free bread, the physician is usually content to have the patient use bread with a relatively increased proportion of protein. This has led to the production in large quantities of so-called "diabetic flours," which are often products of this kind only in name. It is not unusual to find upon the market diabetic flours, so-called, which do not contain any larger proportion of protein than many varieties of good rich wheat-flour. This form of misbranding or adulteration is, of course, extremely culpable; it is undertaken solely for pecuniary gain and violates the very fundamentals of ethics in that it offers under a false name to an invalid a product which instead of helping him does him injury.

Again, some forms of cereals with their natural content of starch have been recommended for diabetic patients. This is particularly true of oatmeal, an article of diet which has been recommended by even so good an authority as von Noorden.

This leads to the inquiry, whether or not different starches may act differently on diabetic patients. If we assume that oatmeal, with its normal content of

starch, is better for a diabetic patient than wheatmeal, with nearly the same content of starch and protein, we must come to the conclusion that there is some one constituent of the oatmeal, presumably the starch, which is more suitable for a diebetic than starches of other origin.

The great importance of the study of metabolism in diabetes mellitus has led to a most interesting and instructive investigation by Francis G. Benedict and Elliott P. Joslin.[11] This contribution is by far the most valuable, from a scientific standpoint of the studies which have been made upon the relation of food to the diabetic patient. One of the points brought out in this investigation is of considerable importance in the study on the effect of food upon diabetic patients, namely, the *respiratory quotient.*

It is possible in studies with the respiration calorimeter to determine the relationship of the production of carbon dioxide to the consumption of oxygen. If, for instance, in the combustion of food in the body the principal product consumed is carbohydrate, the greater part of the oxygen which is used therefor goes to burn that carbohydrate. Hence, if nearly all the oxygen is utilized in combustion, it means that the carbon dioxide produced is largely from carbohydrates, while if the material burned is fat, the quantity of oxygen consumed is relatively low. Thus, if the respiratory quotient were 0.95, it would show that the combustion is largely of carbohydrates; if, on the contrary, the respiratory quotient were as low as 0.72, the burned material would consist largely of fat. The respiratory quotient is the number of cubic centimeters of carbon dioxide produced divided by the number of cubic centimeters of oxygen used up. For example, in the complete combustion of starch or sugar the respiratory quotient would be 1, *i.e.,* the number of cubic centimeters of oxygen consumed is the same as the number of cubic centimeters of carbon dioxide produced. On the contrary, when fat is burned the number of cubic centimeters of oxygen consumed is very much greater than the number of cubic centimeters of carbon dioxide produced, and the same is true of protein. The character of the combustion going on in the diabetic patient, therefore, can be very accurately forecast by the determination of the respiratory quotient.

Benedict and Joslin say (page 231) :—

> **Even in severe cases of diabetes, the determination of the respiratory quotient may have great practical value in showing whether or not the subject is in a critical condition. If in experiments several hours after the last meal the respiratory quotient is above 0.74, it is clear that there is a fairly liberal supply of glycogen or carbohydrate material stored in the body that is actually being burned. . . . The respiratory quotient may also be of very great value in determining the degree of tolerance of the individual for carbohydrate. . . . With a respiratory quotient of 0.70 or below, it is evident that the patient has practically no available carbohydrate, and if previously he has been living upon a moderately liberal diet it is clear that the body has lost in a measure its power of storing any carbohydrate. We may naturally assume, therefore, that the patient may be in a serious condition.**

Still another word must be added to the voluminous discussion of the proper diet in diabetes which has just been briefly summarized. Dr. H. S.

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11 Francis G. Benedict and Elliott P. Joslin: "Metabolism in Diabetes Mellitus." Published by the Carnegie Institution of Washington, 1910.

Carter[12] advises the reduction of the carbohydrate intake to about one-half of the tolerance for carbohydrates as determined by the von Noorden diet. He states as the chief reason for reducing the original intake of carbohydrates to one-half the tolerated amount the fact that the hyperglycemia may not always disappear as soon as sugar ceases to exist in the urine. The hyperglycemia, according to Carter, however, does disappear very promptly if the tolerated amount of carbohydrates is reduced by practically one-half. If, in general, it may be said that a diabetic patient will tolerate 60 grams of carbohydrates per day, then this should also be cut in half, at least for some time, so that the total quantity of carbohydrates per day may not exceed 30 grams.

Diet in Tuberculosis.

The proper diet in tuberculosis is also an important subject about which there is no general agreement. The literature is most extensive and in modern times inclines to the view of a generous and even of a forced nutrition. The dietaries which have been proposed for tuberculosis patients might well be accepted as a basis for the general nutrition of mankind on the most generous scale, and I will read just one table proposed by Dr. Theo. Y. Hull as an illustration[13]:—

	Ounces.	Calories.
Breakfast 7.30 A.M.		
Apple	4.0	53.38
Oatmeal	3.0	50.05
Eggs, 2 (raw)	3.5	134.12
Bread (white)	1.0	73.93
Butter	0.5	107.80
Milk	16.0	312.08
Sugar	0.25	28.35
		759.71
10.30 A.M.		
Egg, 1	1.75	67.06
Buttermilk	8.0	80.85
		147.91
Dinner 12.30 P.M.		
Soup (tomato)	6.0	66.42
Steak (sirloin, broiled)	2.5	187.00
Potatoes (boiled)	4.0	100.34
Peas	3.0	89.80
Bread	1.0	73.93
Butter	0.5	107.80
Sugar	0.5	56.70
Milk	8.0	156.03
Nuts (pecans)	2.0	193.89
Raisins	1.0	87.85
		1119.76
4.00 P.M.		
Egg, 1	1.75	67.06
Buttermilk	8.0	80.85
		147.91

[12] Medical Record, April 22, 1911, vol. lxxix, p. 717.

[13] The Dietetic and Hygienic Gazette, vol. xxvii, April, 1911.

SUPPER 6.30 P.M.

	Ounces.	Calories.
Egg, 1	1.75	67.06
Roast beef (rare)	1.5	139.69
Rice	3.5	104.47
Bread	2.0	147.86
Butter	0.5	107.80
Sugar	0.25	28.35
Milk	16.0	312.08
Orange	6.0	63.43
		970.74
9.00 P.M.		
Milk	8.0	156.03
Total for day		3302.08

The fact that insufficient nutrition predisposes to tuberculosis has long been known. The following verse indicates that as long ago as 1699 this feature of the condition was fully realized:—

> Whilst meager Phthisis gives a silent blow;
> Her stroaks are sure but her advances slow.
> No loud alarms nor fierce assaults are shown;
> She starves the fortress first, then takes the town.
>
> Garth's Dispensary, 1699.

(Thos. S. Blair, "Public Hygiene," vol. i, p. 93.)

TREATMENT OF OBESITY.

The most reasonable principle to be followed in the treatment of obesity from the food standpoint is diminution of the ration, and especially of that portion of it which tends to form fat. Recent experiments in feeding fat meat to partially starved dogs show that large increases in the fat of the body take place, evidently derived largely, if not entirely, from the ingested foods. This, perhaps, would not be sufficient evidence to show that the food was directly assimilated, for in the latter case the nature of the accumulated fat would have to be that of the ingested fat. It is well known, however, that the fat of different animals differs in composition; whence it is not difficult, for instance, to discriminate between the fat of beef and the fat of pork, though both may be produced from Indian corn. From the ease with which ingested fat may be transformed into the fat peculiar to the animal it would seem reasonable, in selecting a ration in obesity, to remove the fat content as much as possible.

That starch and sugar are sources of fat has long been recognized among physiologists. Thus, beeves and pork, in their preparation for the market, are not fed cottonseed oil in this country, but largely Indian corn, containing only 3 to 4 per cent. of fat, from 55 to 65 per cent. of starch, and 1 or 2 per cent. of sugar. The fat which is stored is evidently not derived solely from the oil or fat of the food, because there would not be a sufficient amount of this if all were assimilated to account for the rapid increase of weight under certain conditions. Hence it would be reasonable to suppose that foods rich in sugar and starch, as well as those rich in fat, should be inhibited in a diet intended for the correction of obesity.

The normal weight of man is supposed to bear a certain relation to his height—so many kilograms per centimeter, measured, of course, above or below a given standard. If we assume that a normal man is 5 feet 7 inches in height, we can calculate his ideal weight by diminishing it at a certain rate below this normal and increasing it at a certain rate above; for instance, it may be regarded as a general principle that a man full 6 feet in height should weigh approximately 200 pounds.

Marcel Labbé and Boivin[14] have reported results of experiments respecting the number of calories required in the ration to produce equilibrium in the weight of an obese patient where the tendency to gain weight is very marked. In the case of Patient No. 1, whose weight was 91 kilograms and height 1.55 meters, a diet was given amounting to 2818 calories per day, equivalent to 25 calories per kilogram of actual weight. In a period of ten days on this diet the patient gained an average of 166 grams weight per day. The diet was then reduced to 1830 calories, amounting to 20 calories per kilogram of actual weight, for a month, and on this diet the weight of the patient was practically stationary. The diet was then reduced to 1323 calories per day for two weeks, equivalent to 14 calories per kilogram of actual weight. During this period the patient lost an average of 150 grams per day. In this instance it was seen that a diet equivalent to about 1800 calories kept the patient in equilibrium. It is evident, therefore, that in such a case the diet must be reduced below this amount in order to remedy the excess of weight.

In Patient No. 2, the initial diet was 2228 calories. The weight of the patient remained stationary for a period of two weeks.

In the third case, the patient weighed 94 kilograms and remained stationary on 2501 calories, but this treatment was continued only three days.

The fourth patient, weighing 72 kilograms, gained slightly in weight on 1752 calories.

The fifth patient, weighing 70 kilograms, remained stationary on a diet of 1945 kilograms for two weeks.

The sixth patient, weighing 96 kilograms, showed a slight tendency to increase on 1955 calories per day.

The average amount of food required to keep the six patients in equilibrium of weight varied from 20 to 27 calories per kilogram of actual weight.

These data show that in prescribing a treatment as regards quantity of food for obese patients the actual calorific power of the ingested food should be certainly below 24 calories per kilogram of weight in order to secure equilibrium, and considerably below this in order that there should be a loss of weight.

It might perhaps be concluded from the above that a gradual loss of weight—and that is what is always desired—would be secured, as a rule, by limiting the diet to 20 calories per kilogram of weight. The difficulty in a treatment of this kind, however, is in controlling the will-power of the patient. The temptation to eat when one is hungry is so great that it requires the

[14] Société de Biologie, April, 1911, vol. lxx, p. 529.

greatest self-control and the most patient encouragement on the part of the attending physician to prevent excess in diet. The time has not yet come when we can absolutely predict from the character and quantity of food just what effect will be produced, but we can predict that a general tendency, either to an increase or a decrease in weight, will be established by regulating the quantity of food consumed.

This conclusion is based upon the established laws of thermodynamics, as illustrated by the experiments with the respiration calorimeter. Benedict truly says, in speaking of the quantity of fuel necessary to produce a certain degree of energy:—

> I think figures like these go to show most conclusively that the proposition we hear frequently made to cut down our total food consumption is founded on entirely erroneous grounds. If we do muscular work, we must burn up material. We must draw on body substance or we must supply food. I have no doubt that many of us are too fat, not grossly over weight, but somewhat over. People of sedentary habits have a tendency to take on weight and become 25 or 30 pounds over weight without much difficulty, but I contend that the average man is not too fat, and that his diet is not too large for him.

The converse of this is also shown by the experiments cited above—that if we desire to reduce weight, other conditions being the same, the most effective way is to cut down the supply of food below the normal, the body then proceeding to use up the surplus material which is stored, a consumption of the fatty tissues chiefly. Naturally we do not wish to push a remedy of this kind to actual starvation. A limit must be placed at the point to which the body weight is to be reduced, and this limit of minimum reduction should be approached slowly. There is no doubt, however, in my mind, that nearly all cases of obesity may be controlled by a rigid adherence to a minimum diet until the normal weight of the body is restored. The greatest care must be observed so to order the diet that the quantity of food which is necessary to preserve the body equilibrium is ingested; otherwise the disease which may not have been eradicated by this partial starvation will again become active and the storage of fat again commence.

Chemical Preservatives.

The question of the use of chemical preservatives in foods is one which has been most freely and extensively discussed by many authorities, some favoring and some opposing their use. Foods which are used for therapeutic purposes, it seems to me, scarcely lend themselves to a discussion of this kind, since the physician would certainly not desire to administer drugs in foods in cases of disordered nutrition. Whatever may be said of the use of such drugs in foods for well people, there seems to be no question in regard to their exclusion from the food of those who are ill. Further, it may be said that for prophylactic reasons the arguments in favor of excluding these preservatives from foods in general are well founded. My own views on this matter are so well known as to need no further elucidation.

The only excuse which is usually offered for the addition of foreign bodies

to foods is that they are present in such extremely small quantities. This is a stock argument, the fallacy of which is most easily demonstrated. If one injurious substance, or doubtful substance, may be used simply because the quantity is small, the same right must be accorded to the numerous family of such bodies which now exists, and instead of having one substance in small quantities in foods the final result would be a very large number. That this repetition of slight injuries would result in a great injury is capable of mathematical demonstration. I have used such a demonstration as this in my arguments against the admission of small quantities of preservatives to foods in Bulletin No. 84 of the Bureau of Chemistry. A recent pronouncement on this subject by Dr. James Oliver,[15] Physician to the Hospital for Women in London, is as follows:—

> The incorporation of chemical preservatives with foodstuffs is an ever-increasing evil, a nefarious and fraudulent practice requiring on the part of hygienists the greatest vigilance, and calling for the strictest action on the part of our legislature. Public interest in this very important matter must not only be aroused, but energetically maintained; for quite needlessly, as unwittingly, we are all exposed and subjected to the pernicious influences of these toxic agents; and, insidiously and stealthily, derangement of every function of our bodies may thus be induced. Sufficient protection is not, as has thoughtlessly been alleged, afforded by our legislators fixing a maximal limit for one or more chemical preservatives in a given food; the danger lies pre-eminently in the fact that under such circumstances small quantities of these highly active substances may be ingested with a variety of foods which are in constant daily use, and it must not be forgotten that in our bodies the preservatives themselves or their effects are cumulative. Moreover, on account of idiosyncrasy some individuals are much more susceptible than others to the prejudicial influence of these agents. . . . . It is an undisputable fact that all the modern chemical preservatives are more or less toxic substances, and in an unchanged or changed form the duty of freeing the body of them falls entirely upon the kidneys, which under ordinary circumstances are already overburdened with work, and it is most reprehensible to add needlessly and unnecessarily to their labors.

But these are not all of the evil influences that come from the use of preservatives, for he further says:—

> Every one of the chemical preservatives, when ingested with food, passes readily into the blood and tends to modify and alter the action of every ferment in our bodies, so that metabolism is thereby more or less seriously deranged.

Fads and Fancies.

If the advice given by physicians to their patients respecting a proper diet for disease and convalescence could be collected in a volume it would be a history replete with interest, contradictions, extravagances, dogmas, and absurdities which would constitute one of the wonders of medical literature. The ease with which the physician and so-called "food specialist" predicates certain actions and results from the use of certain foods is only equaled by its lack of scientific accuracy. If a patient should consult five physicians, instead of one, regarding his diet, and each of the physicians should diagnose

[15] The British Food Journal, Dec., 1909, vol. ii, p. 221.

the case alike, the bewildered invalid would be supplied with five dietaries absolutely different in character, contradictory and incongruous. The principal thing of interest respecting prescribed dietaries is, therefore, their lack of consistence. One has only to consult the publications which have been made on uncooked foods, "sun-cooked foods," "nut foods," "sour-milk foods," "vegetable foods," "flesh foods," etc., to get illustrations of the above truths. The effects of this confusion of absurdities perhaps cannot be better illustrated than by a quotation from a letter of the editor of one of our most prosperous magazines, as follows:—

> There are so many of these faddists, so many of these alleged scientists, yapping about the value of this food and the detriment of that food, etc., that I wish you could get time to prepare for us an article exposing the fallacies and the foods with straight-from-the-shoulder writing.

This, of course, would be a hopeless task, and all I propose to do now is to draw attention to this matter and illustrate the point by just a few quotations from those who pose as masters of the science of dietetics.

One of the most frequent of the writers gives expression to the following gems:—

> Sweets are a necessary part of the diet, especially of children, but cane-sugar in any form is objectionable. Honey and fresh dates are the best sweets, molasses candy the least objectionable form. When corn syrup is used it should not be indiscriminately mixed with such heavy foods as beans or pancakes, but is compatible with toast, forming a suitable breakfast for a school boy, if beans and brown bread or corn bread and milk or rice are taken at the next meal.
>
> Milk does not combine perfectly with any other food, but with toast or stale white bread it is better for the average adult than milk alone. Milk is not a natural food for the adult, and the coarse curd of cows' milk is digested with great difficulty by most persons, often putrefying by being delayed in the stomach, on account of faulty motor activity, and causing poisoning.
>
> Consumption is not to be cured nor prevented by being ware of the sputum which may plant the germ in a favorable soil and hasten the process of degeneration. Infantile paralysis will not be cured and prevented by isolating the germ (already accomplished), and finding an antitoxin for it. Degeneration of the central nervous organisms, due chiefly to insufficient muscular exercise, is the essential cause of infantile paralysis. Too early or long standing, maintaining one position, and use of starch foods, tea, or coffee at an early age favor this disease.
>
> When the cells of another animal are introduced through the alimentary canal as food in the form of flesh it is reasonable to suppose that the organism is aroused as when a poisonous substance, like alcohol, is introduced, and perhaps this is the source of the peculiar stimulation which some observe from eating meat, which, although it is easily digested and contains all the elements of nutrition, is open to many objections, of which this is the newest.
>
> Prof. Ehrlich, who is generally recognized as the foremost medical investigator of the day, reports the results of some recent investigations into the cause and cure of cancer. . . . . This confirms, so far as it goes, the nutriopathic theory of the cause and cure of cancer, first announced in this country through these hints more than a year ago. Like many other medical investigators, Ehrlich had a bad school record, failing many times, and, although his biochemical work is brilliant, he had no regular training in chemistry, indicating that, as in the case of Pasteur, Metchnikoff, and other great medical discoverers, who were not physicians, specialization is necessary for great accomplishment in any scientific work.

Uncooked apples, grapes, oranges, pineapple, make a good morning meal for an invalid or infirm person; a whipped egg with well-toasted dry bread for dinner, and rice alone in increasing quantity, as strength returns (no milk, if the digestion be very weak), and buttermilk only or grape juice only in the evening, for which may be substituted prunes (alone), as the strength increases, thoroughly washed. This dietary calls for little vitality, yet contains every element of nutrition, and can be relied up to sustain indefinitely anyone not doing much mental or physical work.

The editor of the Mount Pleasant (Mich.) *Times* reports a case, which I have been unable to verify, of a man living on unroasted Virginia peanuts exclusively for two years, after being declared a hopeless consumptive. . . . . Since peanut fat, uncooked, is very easily assimilated, the only serious objection to such a diet for an invalid is that it is extremely concentrated, being richer than any other food, as the special bulletin issued by the Department of Agriculture on the cultivation of the peanut shows.

Sallow skin, pimples, and blotches of all kinds are produced by failure of liver, kidneys, lungs, and skin to eliminate naturally the waste products of the digestion, whose retention is favored by constipation. The tissues of the body, including the skin, become hardened as age advances, partially by the weakening of these eliminating organs, often prematurely. . . . . These conditions are to be avoided by avoiding constipation and so-called rich foods, by eating few articles of food at a meal, by eating freely of acid fruits, especially apples, lemons, oranges, and grapes, and by the daily use of olive oil or peanut oil, and by the free use of water, including the "internal bath" occasionally. Proper exercise daily in the open air will also serve to preserve a ruddy complexion and soft skin.

"In Rio de Janeiro," says a writer in a recent number of a popular magazine, "in 1888 there was a Spanish physician, an exclusive meat eater, who was then 193 years old." This is doubtless an exaggeration, and is not to be accepted as an argument in favor of an exclusive meat diet, but as additional evidence in favor of the monodiet, the system of eating only one food or a harmonious combination of two or three harmonious foods at a meal, as opposed to the conventional habit of mixing foods indiscriminately, a practice which the invalid especially, the athlete, and the aged who wish to conserve vitality should avoid. I am not sure that an exclusive diet of meat would not be preferable to the incompatible mixtures that many eat daily. The worst mixtures are meat and milk, meat and potatoes or strawberries, meat and sugar, meat with rice, meat with cabbage and some other vegetables. The best combination with meat is whole wheat bread. Fruits, vegetables, and milk should be taken at a separate meal.

It is also true that excess of bile arises from too much proteid or albuminous elements in the diet. It follows, therefore, that healthful buoyancy is promoted by what is termed a "low proteid" diet; that is, restricting to a small percentage the amount of proteid consumed daily—say 10 per cent., sugars (preferably fruit-sugar), starches, and fat constituting the remainder.

Tranquillity of mind is a matter of much importance for the nursing mother. Violent emotion acts upon the milk in a way which sometimes proves fatal to the child. Dr. Carpenter, an English authority, tells of a case in which a quarrel arose between a soldier and a carpenter in whose home the former was billeted. "The carpenter's wife rushed in, wrested the sword from the soldier, and broke it in pieces. While in this strong excitement the mother took up her child from the cradle, where it lay playing, and in perfect health; she gave it the breast, and in so doing sealed its fate. In a few minutes the infant became restless, panted, and sank dead upon its mother's breast."

Henry Q. Mack writes:—

I am just now nearing my 81st birthday, and during all the sixty years of vegetarian living have experienced no prolonged illness. I have led a very active life and

worked down many a flesh eater. . . . . I am as nimble today as when in my teens. Indeed, that condition is identically what the derivative word "vegetus" signifies —lively; animated; vigorous; active; sprightly.

Here is an extract from a letter I received a few weeks ago, which is quite novel:—

In a syndicate article which I have just seen over your name, I observe various comments upon food, and a suggestion for a daily ration, and in reading this I could readily recognize the chemical-magnetic type of your own body, though I only know you by your own expression in the article. I wish to raise the point that your suggestions are only adapted to those people of the same general type as yourself. You are evidently what would be classed by vitosophic science as electric-acid. This calls for warm, sweet (alkali), and quite nitrogenous diet. People who are magnetic-alkali (most Northern women are) would all get constipated on your diet if they live as most city people do. I wish also to suggest that the food bureau could do a great service to the people by showing how much vegetable food is robbed of its value by boiling instead of baking with close covers.

The same author publishes an article entitled "Philosophy of the Sand Diet." He says:—

To my friends and customers: Having taken over the sand sales department of the Boston College of Vitosophy (Western branch) for the time being, I call your attention to my conclusions as to this simple preventive for all of the physical ills that our unwise, careless, or ignorant habits lead us into. . . . .

First: In vitosophic philosophy, earth is the first of the essential conditions of life. . . . .

Second: By keeping the intestines free, the kidneys are saved from anything injurious to them, and thus a very common class of intensely painful diseases is avoided. . . . .

Third: Sand using keeps the skin clean and odorless, causing little soiling of underclothing. . . . .

Our sand is pleasant to take, and, while many prefer to swallow it at once with the help of water, better results are secured by holding convenient quantities in the mouth until the saliva gradually draws it down. By this method, any soreness in the mouth, teeth, or throat is absorbed. No dentistry would be needed if the sand diet was begun in childhood. Some sand ought to be taken after each meal, and if the stomach itself is diseased a full teaspoonful should also be taken on retiring at night to keep the "brown" taste out of the mouth.

The sand in boxes is sold for 50 cents a pound, or three pounds for $1.00. . . .

Filling the nose with sand dissolves secretions and so checks colds and catarrh and can do no harm.

In Suffolk, Virginia, "Aunt Nancy" Shepherd, a mulatto, weighing 80 pounds, who had lived in three centuries, died here early today. She was 112 years old, having been born the year of Washington's death. Mrs. Shepherd's faculties were well preserved. She could see well and her mind was clear, but her hearing was impaired. She was in good health up to last night and ate a hearty supper. "Aunt Nancy" smoked a short-stemmed clay pipe almost constantly, and had partaken of alcohol since girlhood. All her children died of old age.

Following is an extract taken from an article entitled "Old Age a Preventable Disease," published in the New York *Times*, January 29, 1911:—

As is well known in some parts of Europe, notably in Styria, the habit of eating arsenic is very prevalent among the peasants, and it is strange to note that most of these people live to a great age, and at the same time are extremely immune to all

kinds of bodily fatigue—for instance, they can climb the highest peaks in their native mountainous country without great exertion. They take arsenic because it enables them to undertake harder work, such as climbing, with greater ease, and also improves their appearance.

The following is from the literature of a so-called "food specialist" in Washington:—

Expectoration, coughing, colds, night-sweats, constipation, rheumatism, diabetes, tumors, etc., arise from various accumulations derived from wrong foods, unsuitable combinations and proportions, and are cured by the new food system. Special exercises, though helpful, are not essential when living on a suitable brainy diet.

The absurdity of treating typhoid fever by giving a heat-producing food like milk to a person in a warm bed in the height of fever is obvious. No wonder the fever requires so many days to reach a climax, and if not fatal a long time of convalescence, wasting time, money, and life force. When the fever is produced by overfeeding it is cured naturally by cooling fruit and vegetable waters; and when caused by underfeeding, by the addition of meat broth, etc. The patient recovers as soon as the bowels act naturally under the influence of the foods.

It is only proper to add that many of the theories and practices based thereon are so extravagantly urged as to partake to some degree of the nature of the fads and fancies mentioned below.

Fasting, Mastication, and Low Protein.

Dr. Dewey has published a book in which his condemnation of common foods is most sweeping. Milk is especially a *bête noire,* and he fears the irritating effect of fruit acids upon the stomach and maintains that tropical fruits contain no acids. Dr. Dewey cites meanwhile what is well known, that certain neurotic persons, and persons obsessed by the trance habit, can go for long periods without food.[16]

Fletcher's doctrine of mastication has also received much attention. Fletcher follows Dr. Dewey's idea that people eat too much, and also that they bolt their food. The English writer says both are alike in this respect, viz., that they carry principles which are fundamentally correct to an irrational extreme. One of Mr. Fletcher's cardinal principles is that by prolonged chewing not only is the amount of food required lessened, but that which is ingested is more completely absorbed, thus relieving the intestinal canal, which is from 20 to 25 feet long, of the burden of carrying waste material. This idea, however, is contrary to all the principles of the best teachings in physiology, since even in starvation a considerable quantity of fecal matter is poured into the intestines from the consumption of the tissues of the body and because the inactivity of the intestines must of necessity be a constant source of danger. In the tests made by Cetti and Hermann it was shown that when a loop of intestine was entirely severed, and the animal kept alive for a time, it contained considerable quantities of fecal matter, and Praussnitz has demonstrated that a large proportion of the feces is not derived from food residue.

One of Mr. Fletcher's pupils in England, Mr. Higgins, is of the opinion that "the great advantage of finely dividing the food in the mouth, so as to

[16] British Medical Journal, Feb. 12 and 19, 1910.

present as large a surface as possible for the action of the intestinal juices, is obvious when one reflects on the rapidity with which bacteria can and do act on pieces having a small area in consequence of their large bulk. When one reflects that Dr. Mott attributes the main cause of insanity to the absorption by the body of the cleavage products produced by microbes in the intestines, and the increasing recognition of such poisons in the causation of chronic disease and disturbances of health, this factor alone would afford an explanation of some of the phenomena induced by the practice of economical nutrition." There seems to be no point to the argument, however, since by finely dividing the food bacterial action in the intestines is favored, and, as has been established by Cetti, the complete absence of food does not lessen the number of bacteria, but apparently favors their growth in quantities larger than normal.

The writer does not deny merit to Fletcher, but denies that chewing can increase the value of the meat protein; while 60 grams of proteid may be enough for some people, it is yet to be demonstrated that it is sufficient for any large number of human beings.

If any considerable portion of the human race has adopted a diet almost exclusively animal, or, on the other hand, almost exclusively vegetable, it is more as the result of necessity than from choice. Where men have access to all forms of food they naturally eat everything of a wholesome and palatable nature which they can get. There is, perhaps, no doubt of the fact that persons engaged in hard physical labor do extremely well on a vegetable regimen, but it is undoubtedly conducive to obesity in more sedentary employment. For special training in athletics the vegetarian diet has usually been found advisable. In England Mr. Eustace Miles gave some very convincing demonstrations of the value of the vegetarian system, he himself being an athlete of some distinction. With the vegetables, however, milk is usually considered as a legitimate diet, although in point of fact milk is much more nearly animal than vegetable in its characteristics. The vegetarians are also very apt to eat quantities of eggs, as well as milk, cream, and butter and plenty of sauces and flavorings. Cheese also is a favorite diet with many vegetarians, furnishing an animal rather than a vegetable proteid. Prof. McCay compares the amount of work done by a Bengalese vegetarian with a meat-eating Englishman; he says that in cotton spinning in Lancashire a thousand spindles require 4.2 workers, but in Bengal they require 28, and, although the coal in India is thick, soft, and easily cut, the output per miner is 80 tons, as against 287 tons in England. This, however, is not a convincing argument, because there is perhaps a greater difference between an Englishman and a Bengalese than there is between a mixed and vegetable diet. The proper test would be to take a number of Englishmen all of the same characteristics and put them to work upon a purely vegetable diet and upon a mixed and purely animal diet under the same conditions and in the same line. There is no doubt of the fact that health, and apparently strength, may be maintained on a restricted diet, especially a low protein diet, but what the final effects of such nutrition would be one would hardly dare say. Prof. McCay found that the average amount

of protein in the Bengalese diet was 67 grams with 548 grams of carbohydrates and 71 grams of fat, but on this diet 42 per cent. of the workers constantly lost weight. The vegetable protein is undoubtedly less completely digested than the animal, since Prof. McCay found that about 25 per cent. of the nitrogen ingested could be found in the feces of the Bengalese subjects. In regard to cost, it is undoubtedly true that a diet into which alcohol, meat, tea, and coffee largely enter costs a great deal more, without affording any more heat energy or building material, than a similar diet composed largely of vegetable matter.

SUMMARY.

The subject of bromatotherapy is one of such tremendous importance and covers so wide a scope that I am sure you will pardon me for having gone into it at some length, although I must confess most inadequately. Only a volume would do justice to this important subject. I believe that in the future physicians will pay greater attention to the importance of food as a means of healing, and especially as a prophylactic. The general interest in this subject among the people is now widespread and increasing in value and importance. This makes it more readily possible to secure legislative enactments to help the people in their efforts to secure pure food and pure drugs. Yet in spite of all this overwhelming preponderance of public sentiment, there never has been proposed a measure in the National or State Legislature for the protection of the consumer in respect of foods and drugs that did not have violent opposition from interested manufacturers and dealers. The desire for gain is so strong that, no matter how worthy a cause may be, opposition will be developed. Every effort which has been made to purify the waters of the streams by restricting the sale of contaminated oysters has met with opposition. The efforts which have been made to secure a more wholesome egg product, both in respect of age and composition, has met with equal embarrassment and opposition; the efforts to secure pure, unchemicalized flour for the country have had a similar fate; the evils which have resulted from long storage of perishable products in a frozen state have not been remedied without the earnest protests of interested parties, who fear to lose some prospective gain by restrictions of this kind. But the good work goes on all over the country and the world, and the ethical proposition that the people of the country are entitled to purity of food products, to know how they have been treated, where and how long they have been kept, and how much they weigh is firmly rooted and has taken on a growth which cannot be checked. The day is not far distant when all the processes of food preparation will be laid bare before the consuming public, and all the practices which have heretofore resulted in the deterioration, depreciation, or debasement of food products, and their sale under false names and false claims or false weights, will cease.

That food will have an increasing value in the eyes of therapeutists, both as a prophylactic and as a remedy in disease, it seems to me admits of no manner of doubt. It remains for experimental science to determine with greater accuracy the particular functions which are modified by food as a

therapeutic agent, especially to study the effects of foods as specifics in the cause or remedy of certain diseases. The more careful study of infant feeding with a view to supplying a pure, modified milk in place of all the existing infant foods is a matter of supreme importance. The scientific study of diet in certain insidious diseases, such as tuberculosis, demands further experimental demonstrations. The progress which has been made has marked very clearly the lines of investigation which should be followed in the near future.

Bromatotherapy is a new branch of medical science; not new in the recognition of its value, but new in its establishment as a definite course of study. The great medical colleges of the country should seize the opportunity which is now presenting itself to establish courses of study in nutrition, in which the Carnegie Foundation has set a brilliant example, and these studies should be connected with the chairs of therapeutics in order that special lectures may be given and experiments made by the students of the medical colleges in this most important branch of their professional duties. It is but due to the medical profession that the empiricism, bordering sometimes upon quackery, with which the subject of diet has been handled, be removed, and that the educated physician be enabled to give advice to his patient on subjects of such supreme importance in a thoroughly scientific and reasonable manner. It is with the hope that some such general attention will be given to this subject that I have chosen it as the theme of the Presidential Address to the American Therapeutic Society.

NOTE ON FLUORESCENCE EXCITED WITHIN HUMAN TISSUES AS A METHOD OF TREATMENT.

By WILLIAM JAMES MORTON, M.D.,
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I.

Introductory.

Fluorescence.—Fluorescence, as commonly stated, is the property which substances possess of absorbing invisible or visible rays and giving out in turn visible light. Phosphorescence is the same phenomenon persisting after the exciting agency is removed. But we may now go further than this, for *invisible* fluorescence has been discovered, both in the infrared and in the ultraviolet regions. And, indeed, it is only natural that this should be so, for why should it exist only within the narrow limits of the visible spectrum? In brief, the fluorescent or phosphorescent material receives the impact of various radiations, visible or otherwise, and gives out another rate of vibration of the ether, also visible or otherwise.

Ordinarily, shorter waves are transformed into longer; but the reverse may be true. Ordinarily, too, the transformation is within the scale of the visible spectrum, but here again, as pointed out above, resultant wave lengths exist beyond both the red end and the violet end of the normal visible spectrum.

Some substances are both fluorescent and phosphorescent; some, under both conditions, have the same color, while others present a different color. According to Koblentz, the material acted upon is a changer of the frequency of ether vibration. But here again we may take an important step forward, for Prof. Wilder D. Bancroft, basing his theory upon some beautiful chemical experiments, maintains that as a matter of fact the ether waves are not changed directly into waves of different lengths, namely, that it is not a question of "frequency changing" as heretofore assumed, but rather that the ether waves produce a chemical change or changes which in their turn cause the emission of light. It would now seem that we are getting on solid ground as regards these heretofore somewhat elusive phenomena of fluorescence and phosphorescence, for, whatever the atomic mechanism concerned in the emission of the new radiation may be, its primary cause is chemical excitation and not radiation transformation.

Fluorescent and Phosphorescent Substances.—A few of the fluid or soluble fluorescent and phosphorescent substances which may be found available for therapeutic work are: quinine, esculin, fraxin, eosin, fluorescin and its sodium salt, uranine; rhodamin, resorcinol, cochineal, copper potassium chromate, gentian, henbane, litmus, naphthalene red, paraffin, petroleum, petrolatum, stramonium, turmeric, indigo, safranin, pavlin, magdala red, thallin,

resorcorufin and resorcinol blue, some salicylates, anthracene, mercury bromide, cupric iodide, sodium and potassium iodide, etc.—a long and increasing list.

At present simple temperature radiation is produced at great expense. The time is probably not far distant when the inexpensive and "cold light" of the glowworm or of the firefly may be duplicated for commercial illumination. Already the physicist in his laboratory is bending his deepest thought to find some way of solving this problem. So also in our medical practice these fluorescent and phosphorescent phenomena may be summoned to our aid. Indeed, I am now prepared to say that these phenomena are reduced, in the light of a procedure I am about to outline (and previously outlined in 1904), to a therapeutic practice quite as exact as the ordinary stomach dosage of opium, calomel, quinine, and other drugs. We now see but the beginnings of this medical utilization, but I will prophesy that their proper interpretation in relation to the cure of disease will convey a profound meaning to the medical science of the future.

Excitants of Fluorescence.—The most familiar of these are sunlight, the various electric arc lights, the Cooper-Hewitt mercury lamp, the disruptive discharge of high-tension electric currents, the Röntgen ray, and radium. The excitants I would at this moment call attention to are the X-ray and radium, because of their deep penetration into tissue.

II.

A Therapeutic Method.

We may now combine the two factors thus far alluded to, namely, the fluorescent substance and the excitant, into a method to be practised within living animal tissue, *i.e.*, within the patient's tissues. Granting the innocuousness of the form of excitant radiation to be employed, the first thing, of course, is to discover equally fluorescent media which may safely be introduced into the animal organism without toxic or other harmful effects. One of the most obvious of these is *quinine*, the fluorescence of which is bluish. A far more powerful and at the same time an innocent fluorescent, giving a vivid and rich blue color, is *esculin*, derived from the inner bark of certain chestnut trees. The substance I have especially employed has been *fluorescin*. I use a standard solution of this substance—1 part to 30 parts of water—and of this solution I administer 10 drops three times daily in a full glass of water one hour after meals, often carrying the daily dose up to 40 drops three times daily. With a minimum dose the patient's urine and saliva, or the serous discharges from an open wound, are demonstrably fluorescent to ordinary daylight. The effect is cumulative, and the patient's fluids remain fluorescent some considerable time after the discontinuance of the medicine. The fluorescent color of fluorescin is a beautiful yellow-green resembling that of the glowworm.

There are many other harmless substances which may be used in the same manner. Many of these are the so-called "coal-tar products." How many there are whose response to the excitant is beyond the ultraviolet or infrared range of the spectrum, I do not know;—probably there are a great

many. *Iodide of potassium* and allied *iodides* and *bromides* may be kept in mind as suggestive.

But, I do not wish to take up *in extenso* this branch of the subject in this paper. I have already amplified it in other publications. I would return rather to the basis of the method. This consists in saturating the patient's blood and tissues with some one of the harmless fluorescent substances alluded to and then submitting this same patient, in whole or in part, to any one of the exciting agencies above named. The effect upon the cells would thus be such an effect as would be produced by different varieties of light, by the chemical and invisible rays of the ultraviolet region, or by the longer wave-lengths of the ultrared region. Or, to be more exact, the primary effect would be that due to the rate of ether vibrations of the visible and the invisible spectrum, while the secondary effect would be to produce an increase of oxygen in intimate relation to tissue atoms and molecules.

To be a little more explicit as to the relation between the fluorescent substance in the tissue and the excitant, I would point out that it is self-evident that wherever the patient's tissue may be penetrated by the exciting agency of ordinary sunlight, by artificial light, or by the Röntgen or radium radiations, the new or transformed fluorescent light will be produced at that point and within the tissue. If, for instance, an ordinary electric light bulb be grasped by the hand, anyone can see that light penetrates the flesh. If this flesh be saturated, for instance, with fluorescin, and sunlight, or radium, or the X-ray be used to penetrate the flesh, it will be bathed in a yellow-green light; if esculin or quinine be employed, the tissue light is bluish.

If we go a step further and X-ray a patient saturated with fluorescin, the entire patient, wherever the rays penetrate, is permeated by the yellow-green light. If, on the other hand, it is desired to restrict the light effect to a smaller area, as, for instance, a lupus or an epithelioma upon the face, the entire patient is saturated with the fluorescent substance and the radium or the X-ray applied locally, thus producing merely a local fluorescent effect. I do not mean to say that in the patient's case the hand or the body will appear to our eyes to be of yellowish-green, or of blue, or of any other particular color. This shade is obscured by the overpowering red color of the blood. What I do mean to say is best illustrated by a comparison, as follows: The amount of fluids (blood or other fluids) in an adult human being is about 16 pints, or 2 gallons. Let us add 10 minims of a solution of fluorescin (of 1 part to 30) to 16 pints of water and expose this slightly colored water to ordinary daylight. It is vividly fluorescent. Substitute the X-ray or radium for daylight, and again the 16 pints is fluorescent, or, at least, the parts of it exposed. Substitute the patient for the bottle of fluorescing mixture, and the patient's fluids fluoresce. On a small scale the experiment is easily made in a darkened room. A transparent tube of celluloid (glass itself fluoresces) contains a very dilute solution of esculin or fluorescin. Introduce into the fluid a tube of radium, and the fluorescence is shown. The facts, therefore, are easily established.

In connection with the degree of effect produced, it must not be forgotten that the tissue molecule and the fluorescent light are coincident in space, *i.e.*,

that there is no loss in the intensity of the especial light by reason of distance, as would be the case in ordinary phototherapy, which at the best can only act at the very surface of substances. Again, it must be borne in mind that the ultraviolet region of the spectrum exerts its most powerful chemical action when it can be brought to bear, as in this instance, at close quarters. Von Helmholtz, on illuminating a solution of quinine sulphate with the ultraviolet rays, saw a bluish-white light proceeding from all parts of the solution which were acted upon by the ultraviolet rays.[1]

An influence is also exerted by the infrared rays. Although invisible to our senses, photographs presenting remarkable characteristics may be taken by both of these rays. Such photographs show us black where our eyes see white, white where we see green, window glass opaque, light tones where we see black tones, as in the case of printers' ink, and, finally, shadows feeble or absent. This I mention to remind us that (as is true in the method I am outlining) a state of things may exist which corresponds to realities quite beyond the grasp of our senses, such as they are. We are dealing, in these fluorescent substances, with no mean forces.

So impressed was I by the reasonableness of what is involved in the foregoing remarks that in 1904, at the Electrotherapeutic Section of the International Electrical Congress of St. Louis, I read a paper entitled "Fluorescence Artificially Produced in the Human Organism," etc. My present hope is to call renewed attention to what I believe to be a rational therapeutic method.

III.

Applications to Disease.

A paramount question is, What effect is produced upon tissue-cells by radiations or irradiations such as we have been discussing? From this starting point the clinical effects must be deduced.

A primary effect of these radiations would seem to be to produce an increase of oxygen in intimate relation to tissue molecules. A secondary and clinical effect of these radiations (and doubtless of all others) would be to promote and intensely increase the normal intracellular changes, viz., to accelerate the normal cycle of cell activity. Thus, an intense catabolism is established, and the cell, pushed beyond its capacity to keep up with these rapid interchanges, dies or becomes disabled. This is why cells whose intracellular changes are naturally very active, such as epithelial and embryonic tissue-cells, are remarkably susceptible to the Röntgen and radium rays. Naturally active, they are the more easily pushed to an activity greater than they can survive under. The final result, therefore, of intense radiation is to arrest the progressive processes of both normal and pathological cells.

I have purposely said "of *intense* radiation," as I wish to draw a sharp line of demarcation between degrees of radiation. For the moment we may divide radiations produced by the same agency into mild and intense. These distinctions may be ascertained not only physically, but clinically. And I wish

[1] Landois: Sterling's "Physiology," p. 981.

to say right here that in my opinion nothing has done more to obscure the medical results of radiotherapy than the failure to draw and to keep in mind this distinction. My point may be made clearer by a rough comparison with a rubber band. By overstretching, or stretching oversustained, the elasticity of the rubber band may be lost. Such are the results of intense radiation. Or, again, take any normal function of the human body. By being overdriven the function is lost; by proper use the function is bettered; indeed, remains at the normal. So it is with the cell: intensely rayed, it dies or is subdued; mildly rayed, its function is promoted. A mild radiation (hard tube, short time, and long distance) is highly promotive of the growth of the hair, of the nails, and, in short, of all cell growth. An intense radiation (soft tube, longer time, and shorter distance) is one of the most destructive agencies to cell growth known to science.

Now, the greatest drawback to definite results in Röntgen and radium radiotherapy has been, and is, the difficulty of apportioning the dosage to different depths of disease. When the disease is superficial the problem is no problem. But when it is deep, the intervening tissue acts as a filter—absorbs even dangerously the radiation, and delivers, perhaps, to the internal parts to be treated the mild or stimulating ray when the non-stimulating and growth-inhibiting ray might be desired. It is at this point that the fluorescization of tissue I am suggesting comes into play. The X-ray or radium radiation, filtered out to a minimum, still excites the fluorescent material, now a fluid part of the tissue, and the new rate of vibration acts. The case is parallel to that of a fluorescent screen laid face to face upon the negative plate before the ordinary Röntgen exposure;—a part of the result upon the negative plate is attained by reason of the fluorescent light of the screen. In fact, the result is greatly intensified. In calling attention to the effects upon cells and tissue of X-ray and radium radiation, I do not wish to be understood as in any way appealing to these radiations as explanatory of the effects produced. Be these what they may, and there is no doubt as regards their existence and their utility, my desire is to point out that there is a fluorescent radiation which is easily produced, and is efficacious, in its turn, in bringing about effects of its own.

In support of this is the multitude of facts ascertained as to the effects of light both in the animal and the vegetable world. Under the influence of the sun the intervening fluorescent chlorophyll stores up a supply of carbon. In the animal world why should not the intervening fluorescent substances store up oxygen? And let it be remembered that the light I am speaking of is located *in* the cell itself. I would, therefore, claim a new process of fluorescizing cells, and that to that process distinct results in the cure of disease are due.

Special Applications in Treatment.

Fluorescization.—The general principle once grasped and admitted, it would seem that it would apply to every therapeutic radiation treatment; and this is the fact, whether we employ sunlight, high-frequency electric discharges, the mercury lamp, or the Röntgen rays and radium. But the two latter, by

reason of their greater penetrative powers, would seem to be specially indicated as excitants. In all cases of cancer treated by Röntgen and radium radiation I have continuously employed the method since 1903. What success I have met with I consider has been contributed to in great measure by the fact that the patient has been continuously saturated with a harmless fluorescent solution during the course of treatment.

The same is true of lupus. Fluorescization exerts a most favorable influence upon tuberculosis of the bones, upon tuberculous glands, and upon tuberculous manifestations of the inner organs in general, as, for instance, in peritonitis, cystitis, and tuberculosis of the lungs. The favorable influence of the Röntgen ray alone upon tuberculosis has been noted by Escherich, Lancaster, Bazy, Kirmisson, Béclère, Sainton, Leigh, and notably Freund in reported cases. My own observations over a number of years lead me to believe that an accompanying fluorescization of the affected tissue has greatly enhanced the rapidity of cure in many superficial and not deeply seated lesions of a tuberculous nature which I have treated with success. An interesting research would be to extend this treatment to vertebral caries of tuberculous origin.

But I will not enumerate further. It is not my intention to outline a specific for any one disease, but rather to outline a *method,* in my mind so simple, so obvious, so well based upon scientific principles, and so generally applicable to many diseases and morbid conditions that the merest tyro in radiotherapeutics may practise it—greatly, I believe, to his own and to his patient's advantage.

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THE DELUSION OF THE TONIC AND STIMULANT EFFECTS OF ALCOHOL.

By T. D. CROTHERS, M.D.,
Superintendent of Walnut Lodge Hospital,
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This subject is one of unusual interest, and lies along the great borderland of medicine, where traditions, delusions, misconceptions, and ignorance join scientific research, accurate study of facts, and conclusions that are beyond all controversy. Thirty or more years ago alcohol was considered a stimulant or tonic, and was used freely without question or doubt. The textbooks of that and of earlier periods urged that it was a most valuable agent and practically indispensable in the treatment of disease. Today alcohol has no place in practical medicine as a stimulant and tonic. It is known and recognized as an anesthetic and narcotic. The ethers of alcohol are simply invaluable and have done much to make rational medicine what it is. The most marvelous surgical advances of the century have followed the recognition and application of these alcoholic ethers, and the end is not yet. There are possibilities of farther discoveries and practical applications that are at least startling.

The modern physician regards with astonishment the theories and delusions of the past, in mistaking the effects of alcohol for those of a stimulant and tonic. He is equally startled to note that physicians of eminence and authors of textbooks, and a decreasing number of writers, still adhere to the delusive theories that alcohol has some tonic and stimulant effect. Exact research and a study of the facts have convinced the great body of the profession that physiologically alcohol is a depressant and anesthetic, and, while there is much confusion, the facts are accumulating with such rapidity and clearness that there can be no other conclusion.

Historic Conception of Alcohol.

Many of the old Grecian philosophers declared that wine was a depressant, and never to be regarded as a stimulant giving new powers and activities. Long ages before this the same idea had been mentioned, and it is found in inscriptions on the papyri and the walls of the tombs of the early monarchs of Egypt. One of these statements, dating back over 7000 years, refers to wine as lowering vitality, shortening life, and driving out the spirit from its tenement, the body. Another papyrus contains the statement that wine drowned the victim and failed to rescue him. In Ebers's papyri and in the recently published "Book of the Dead," there are distinct references to the depressant and sleep-producing action of alcohol, comparing it with the poppy juice. This was the statement of the medical priests seventy centuries ago.

The delusion concerning the effects of alcohol was fostered in the palmy

days of Grecian civilization, when wine, song, and art were all regarded as synonymous. Spirits were supposed to liberate the highest powers of the mind from animal impulses and bring out the best thoughts and the most spiritual expressions of art, song, and literature. This delusion has come down through the ages as a fact, accepted beyond question, and today is indirectly taught and supported in literary circles. Wine and spirits are still deified as agents to give power and strength, and in some way increase the higher mental faculties and elevate ideals of life.

There have been protests and denials through all the long centuries. Every now and then someone would assert that this theory was untrue, and that alcohol in any form was incapable of developing the brain or body. In Roman times a number of authorities discerned this fact and asserted positively that the action of wine was degenerative and depressing. This view was repeated down through the Middle Ages, over and over again, and the Grecian authorities were appealed to to confirm it.

During the eighteenth century Condillac, a French philosopher, contended with great force and clearness that inebriety was a disease, and that alcohol was a depressant, destroying mental and physical activities. The disease theory was materialized at Binghamton, in 1860, in the first inebriate asylum in the world.

Scholastic teachers in literary colleges and other institutions still asserted that wine and alcohol had some power to revivify and develop the brain and body, and, when asked to account for the bad effects, explained them by theories of adulteration and dosage. When such theories were submitted to a scientific test they could not be sustained. The most enthusiastic supporters of alcohol as a medicine were constantly confronted with the failures of scientific study to support their clinical experience. Thus tradition and delusion came down through the centuries, promoted by scholastics and unreasoning literary and scientific supporters.

Another view of the subject is presented in the

Results of Laboratory Studies and Exact Scientific Research.

As early as 1845, when alcohol was beginning to be used as the great stimulant drug in disease, a number of observers denounced it and called it a depressant and narcotic. Several English physicians in the sixties and seventies denied that it had any stimulant or tonic action, basing their conclusions on studies and comparisons of cases treated. Laboratory work began about this time, and the enthusiastic claims of the value of alcohol as a medicine were found to be unsupported by laboratory researches. Dr. Richardson, in his Cantor Lectures in the seventies, called attention to the depressant and anesthetic action of spirits, and explained their peculiar fascination and delusional effects as due to this action specifically. Attention was thus called anew to the supposed value of alcohol in medicine, and a number of eminent men opposed the claims of its supporters.

Finally, Kraepelin, of Heidelberg, took up the subject. He assumed

that if alcohol in its physiological action on the body was a stimulant or tonic this effect could be most readily seen in a study of the senses. Under the influence of alcohol the latter should show greater acuteness and strength, which could be measured by instruments of precision. He selected a number of healthy total abstainers, principally students, and made accurate measurements of the senses for a period of many days, in order to secure an average of the normal condition of each one. With this as a basis for comparison or control experiment, he gave to each one at intervals of one or two days small doses of ethylic alcohol of known purity and strength. From forty to sixty minutes after the alcohol was taken careful measurements of the senses were made and tabulated. These experiments were continued over a period of two or three weeks, and the results of the measurements compared with those in the normal condition. It was found that in no instance did alcohol, even in dram doses, increase the activity or acuteness of the senses, but, on the contrary, that it invariably depressed them. Thus, the sight, hearing, smell, taste, and touch were all deranged and lowered to an extent that was measurable by instruments of precision and could be stated in exact terms. This condition followed in less than an hour after the spirits were taken, and there were no exceptions; in no case did alcohol act as a stimulant on the senses, or even as a tonic. There was an exactness in this study which could not be mistaken, and its repetition since that time, in many laboratories and in practical work, has been confirmatory.

Over a dozen different observers have taken up this subject, first finding some normal condition of personal equation and then giving spirits and comparing the effects with the condition that had existed before. One of these studies was a measurement of the muscular output of laborers and workmen with and without small doses of alcohol. At the first, irritant effects were evident in all cases. The heart's action was increased, the blood-tension was raised, and there was an apparent increase of muscular power; but this was convulsive, of short duration, and followed by great depression, so that the output of work was greatly lowered instead of being increased. Alcohol was shown to diminish muscular energy, increase fatigue and feebleness, and in no way could be called a stimulant or tonic. Very curious and suggestive studies were made to determine the action of alcohol on the mind and nervous system.

Time-reaction, ability to discern impressions made on the senses, and to reason as to their significance, was found to be always diminished, and to an extent that was measurable, even in small doses, where the personal equation had been eliminated. There were slowness of thought and mental activity, loss of control and ability to recognize sudden unusual conditions. The memory was enfeebled, and this was measured and shown to be the direct result of the anesthesia of spirits. The heart's action was increased, and with it the circulation of the blood in the brain. With this there were confusion and want of clearness, control, and power of concentration, in some cases very evident, in others less so, depending on some unknown conditions. The apparent stimulation was simply irritation, and not increased power or capacity.

A great number of experiments have been made along these lines, evidently by persons who were not sure that the theories of the past were unfounded.

One very extensive experiment was made with typesetters in a government printing office in Germany. Alcohol was given in small doses at intervals and the output was measured with great care. Sources of error were eliminated, and the results found were increased errors, lessened work, greater exhaustion, and a measurable anesthetic action. Alcohol did not increase the ability to set type or give the men greater tonic powers to continue the work. The same elaborate experiments were made among sharpshooters in the army. The object was to determine whether small doses of spirits increased their accuracy and efficiency. Comparisons of persons, both abstainers and non-abstainers, who were given small doses of spirits before the trial, and under exactly the same conditions, during a period of many days, showed the same results exactly,—depression and anesthesia. In all there were lowered sight, deranged muscular activity, and enfeebled power of control, and the accuracy of the work was greatly diminished.

In this country, under the direction of Dr. Kellogg at Battle Creek, a great variety of similar experiments have been made, confirming and verifying the results of the European observers, and showing the same physiological, psychological, and pathological depression and anesthesia, leading up to final paralysis. Dr. Hodge, of Clark University, showed that alcohol produced degenerations and retarded muscular and mental activities in animal life, and his experiments have become classical, as demonstrating the anesthesia and cell disturbances resulting from small quantities of alcohol. Recently Dr. Downs, of Philadelphia, has published the results of some very striking experiments on the action of alcohol on the heart muscle. Small doses were shown by the tracings not only to depress the heart's vigor, but to derange and lower its activity.

These are only a few of a great number of exact studies that have been made in this country and Europe for the purpose of determining whether alcohol has any real stimulant action on the normal activities and functions of the body. The conclusions were substantially the same, and in no instance was there any support to the theory that alcohol imparts new vigor, or is really helpful as a tonic, either medicinally or in any other way. The literature on this subject has become quite prominent in both pamphlets and books, and the facts and the evidence on which these writings are based are constantly accumulating in the laboratory. The value of alcohol as a food is questioned with equal exactness, and, while still contradicted and the subject of considerable confused thought, research seems to have but one conclusion, and that is, that the effects of alcohol are depressant, corroding, eroding, and toxic, and without any value other than that of an anesthetic.

Evidence still more conclusive has been slowly accumulating from

Clinical and Statistical Studies.

It is a curious fact that a large part of the literature regarding the value of alcohol as a stimulant and tonic is based on tradition, personal opinions,

and the superficial views of many good men whose scientific acumen rests on prejudices and preconceived views. The teachings of prominent authors are accepted without question. Thus, Todd, Bennett, and other clinicians who wrote praising alcohol for its stimulant and tonic action made an army of converts, who accepted their conclusions without hesitation. No one seemed to question the accuracy of their conclusions, but, on the contrary, eagerly sought to confirm them in every way possible. Even today physicians of the older school insist that these early teachings are true and that their experience has proved this.

One of the first breaks in this delusional evidence was furnished by mortality tables which showed clearly a higher death rate where alcohol was used as a tonic or stimulant. In pneumonia, according to the old theory, the stimulant action of alcohol on the heart was essential, and yet comparisons showed an increased death rate wherever it was used. A number of recent authors have asserted that statistical studies showed that alcohol could not be a stimulant and tonic. In the treatment of diphtheria when alcohol was given as a germicide and heart sustainer, the mortality rates and the complicating diseases were increased and the entailments following far more serious. The same facts were brought out in a study of tuberculosis, with the addition of diminished duration and greater intensity of the symptoms. The apparent improvement ended in sudden and unexpected collapse and death. Alcohol is still used by some authorities, but the reasons for and the results of its use are most unsatisfactory. This clinical experience has been accumulating rapidly, and has been tested in many ways, and in no instance has alcohol as a stimulant or tonic been sustained. In the various forms of anemia and neurasthenia some notable comparative studies have been made with and without alcohol in the treatment. The conclusions were unanimous that the use of alcohol increased degenerations and congestions, and encouraged various forms of toxemia which did not exist before, and hence was a dangerous remedy. Alcohol, so strenuously used in the past, and urged even today as a tonic for children or old people, is found to increase the metabolic derangements of the body beyond any question or doubt.

A few years ago a curious controversy occurred in a city in Europe in which a hospital physician was charged with neglect in failing to use alcohol in pneumonia. A formal trial followed, in which the opinions of leading clinicians of the country were found to be unanimous in condemning alcohol as a specific for this disease, so that the failure to use it was not to be considered a fault or neglect of the physician. The result of a somewhat acrimonious discussion showed that it was very doubtful whether alcohol ever prolonged life or shortened disease, but that it was very certain that the opposite followed in most cases, and that a physician was under no responsibility to use it as a drug. Curiously enough, the physician who was the leading prosecutor of the doctor who refused to use alcohol in the pneumonia cases in the hospital was himself charged with malpractice for using it so freely, and the high mortality rate of the hospital over which he presided was presented as evidence. The subject was then rediscussed, and the conclusion reached that alcohol should never be

used as a stimulant or tonic in preference to other drugs whose effects are uniformly certain.

Many very interesting papers in this country and England have called attention to the fact that alcohol is a very dangerous drug in collapse states, particularly following typhoid fever, stating that, while there would be an apparent resuscitation for a short time, the succeeding depression more than compensated for the slight exhilaration, which ended in more serious collapse and death. In shocks, concussions, and sudden comas followed by collapse the use of alcohol rouses the heart to intense activity for a brief time and sends an increased volume of blood to all parts of the body; but there is sure to be a reaction, which frequently ends fatally. If the coma is the result of a ruptured blood-vessel, nothing can be more fatal than to irritate the heart and send a greater force of blood through the opening. The supposed stimulant action of alcohol is then fatal. In concussions with coma the same result follows. In depression of the vasomotor system and convulsive derangements of the circulation, the increase in the arterial tension and its sudden fall following the use of alcohol afford unmistakable evidence of its danger.

Hospital statistics furnish the best evidence of the delusion of alcohol as a stimulant or tonic. The widely different results of treatment where alcohol has been abandoned must be due, in a large measure, to this fact. The explanations given ascribe it to other causes, such as nursing, more exact use of a great variety of means unknown before, etc., but there is unmistakable evidence that the disuse of alcohol as a stimulant or tonic accounts for it. One noted specialist still insists that alcohol is a stimulant and germicide, and is very largely oblivious of the frequent comparisons of the results of his treatment with that of others who do not use spirits, either in hospital work or general practice.

Chloroform and ether represent the exact physiological effects of spirits in all forms and doses, differing only in degree. The exhilaration and irritation preceding the anesthesia are the same. They may be very brief or of long duration, but their character is identical in the action of every form of drink in which spirit is the basis. The first effect is irritation, excitement, and this may be very short, but the second effect of depression is sure to follow. Therefore, clinical studies most amply confirm laboratory researches and conclusions, that alcohol in its action on the tissues in health or disease is purely an anesthetic and narcotic. The fact that the heart is roused to greater activity is not evidence of new force or power. The effect of this impetus, extending to the nervous system and acting in a convulsive way, indicates derangement and paralysis rather than stimulation and increased vigor. The scholastic tradition and delusion that alcohol in some form will bring out some quality of the brain not existing before, or will give strength and vitality, should pass away as unsupported and incorrect. To imagine that spirits loaded with ethers, taken as a beverage at a banquet, will rouse into activity latent forces not otherwise available is equally fallacious.

Some conclusions may be stated with great positiveness: *First.* Alcohol is an anesthetic, dehydrating, depressing toxin. Its apparent stimulation is

irritation,—a convulsive, tetanizing exhibition of energy, associated with and followed by depression, diminished vitality, and loss of motor and sense impressions.

Second. In disease it is a toxin, acting on nerve-cells and nerve-centers, checking their normal activities, and deranging and breaking up their movements of growth and elimination.

Third. The toxicity of alcohol is general, beginning with depression, lessened vitality, and feeble resisting power. It limits and destroys cell life in an unknown way and degree, and is cumulative, uncertain, and dangerous.

Fourth. Like other delusions in medicine founded on misconception and false reasoning, with the accumulated prejudices of ages, the erroneous idea of the action of alcohol continues tenaciously, dying very slowly. The bar of scientific research calls in question the evidence and demands the facts on which the ideas are based, refusing to accept the theories and traditions of the past unless they agree with the teachings of science at the bedside and in the laboratory.

The decision that alcohol is not a stimulant and tonic has been pronounced, and yet the delusions of the past still echo in textbooks and medical papers like the far-off sounds of belated travelers.

DISCUSSION.

Dr. Alexander D. Blackader, Montreal: We have listened with much interest to the powerful presentation by Dr. Crothers of the arguments to prove that alcohol is not a stimulant and not a tonic. Although my name is down on the programme to discuss the paper, the hour is so late that I think it would be inadvisable to do so. In passing, I merely place myself on record as belonging to the old school who still think they see benefit not infrequently arising from the use of alcohol as a prompt, although fleeting, stimulant. In prolonged pyrexia it conserves nutrition and is utilized as a food. The time has not yet come when we can altogether dispense with alcohol in our Pharmacopœias.

Dr. F. E. Stewart, Germantown, Pa.: I agree with Dr. Crothers that alcohol can no longer be regarded as a stimulant. It belongs to the methane group, and, like other members of the group, is a depressant. Also, like other members of the group, it possesses anesthetic properties. It is very valuable in that it does good work in this respect.

SOME OBSERVATIONS ON VACCINE THERAPY

By EVELYN WYMAN NAGLE, M.D.,

BOSTON, MASS.

At the annual meeting of the Laryngological, Rhinological, and Otological Society last spring I read a paper on "The Results of Vaccine Therapy in Chronic Suppurative Ears." I reported 40 cases. In 6 of these the discharge had been present several months, but they had resisted all the usual methods of treatment, and the discharge was so profuse that I considered them suitable for inclusion in the list of cases, especially as my one failure came in this class. In the other 34 cases the ears had been discharging all the way from one year up to forty years. Out of the 40 cases there had been only 1 where the vaccine failed to cure the discharge, and I am at a loss even now to account for that especial failure, for the discharge contained a pure culture of staphylococci, and I had an active staphylococcus vaccine. Some of these cases were treated two or three years ago.

In the discussion that followed my paper I was greatly interested in hearing that some of the physicians had tried vaccines, and that some had had no success with it, and the others but little. It seemed to me that the reason for their failure must have been either an inactive vaccine or wrong dosage, or possibly the length of time that elapsed between the injections; and as these are three very important factors in the treatment, I thought it might be of interest to this Society if I explained the technique of the preparation of vaccine at greater length.

To secure an active vaccine one must have a virulent type of bacteria; these must be killed at the correct time, before they begin to lose their cultural characteristics, and it is essential to subject them to the lowest degree of heat for the shortest possible time necessary to kill them. The discharge from which the vaccine is to be made should be smeared thickly over the surface of the culture-tubes, and the tubes are then incubated at the temperature of 37° C., until the growth has nearly reached its height. The time of incubation varies in accordance with the rapidity of growth of the different bacteria. When the height of the growth is nearly reached the cultures are washed down to the bottom of the tubes, off the surface of the media, with normal saline solution, under sterile conditions, and collected in one tube. This tube is then sealed with the blow-pipe and subjected to the lowest temperature that will kill the organism, for the shortest period possible. The vaccine is then tested to see if it is sterile, and, if not, the tube is sealed again and subjected to more heat. I always feel that a second sterilization is detrimental to a vaccine, and, if possible, I get more pus and prepare another vaccine, using the one that has been sterilized twice until the new vaccine has been prepared.

After testing the vaccine and finding it sterile I count and bottle it. I

put up my vaccines in sterile bottles holding 25 c.c. In case of staphylococcus vaccine, each cubic centimeter represents 600,000,000 bacteria, while in vaccines of all other bacteria the cubic centimeter represents only 100,000,000. The bottles are sealed with an inverted rubber nipple. The well that is made by inverting the nipple is filled with absolute alcohol, to sterilize it, before the aseptic hypodermic needle is pushed through to draw out the vaccine. I make it a practice always to test my vaccine once again after it is all bottled, to see that it is truly sterile before it is injected into a patient. I have known of cases where the vaccine that was being used was tested only once and then injected into the arm of the patient, with the result that an abscess formed at the site of the injection. When this vaccine was tested again it was found to yield a growth on culture media after being left in the incubator two days. The sterilization of the vaccine had changed the characteristics of the bacterium, making it a much slower grower than it was originally. Sometimes the vaccine may become infected while sealing the bottle with the rubber nipple.

The question of dosage is a difficult one. I do not depend on the opsonic index, but rely entirely on the clinical symptoms. Usually my initial dose is a small one, a quarter of a cubic centimeter (150,000,000 bacteria in case of staphylococcus vaccine), increasing to a half, two-thirds, and then a full cubic centimeter, and continuing with this dose if there has been marked improvement. Sometimes it is necessary to increase the dose to 2 c.c. before there is improvement. In such cases I usually prepare another vaccine, making it of double strength, so that there will not be such a large amount to inject into the arm and to be absorbed. There are some cases where I do not increase my dose gradually, but after the first small dose I give a large dose at once: cases in which it seems imperative that the patient should be quickly brought under the influence of the vaccine, as in the event of recurrence during treatment. In cases where vaccine is given oftener than twice a week, I give smaller doses. I think the dosage is something that has to be studied, and one must feel one's way along according to the systemic reaction. After symptoms have subsided I decrease my dose, and continue with this decreased amount for six injections. At first I used to decrease the dose rapidly, but I soon found that this method was unsatisfactory, because the symptoms recurred. I seem to get the best results by giving the patients injections at intervals of three and one-half days, as a rule. If the patient misses an injection I return at once to a beginning dose, in order to avoid a marked general depression with a great deal of local reaction in the arm. In the case of one of the patients who felt a depression about half a day or a day before her next injection, I decreased the length of time between her treatments with very happy result. Another case seen last spring was one in which both ears were discharging freely. She was at once put on vaccine. After eight injections one ear was entirely dry, and the other had only a slight moisture in it. She was getting her vaccine about twice a week. The patient was then obliged to leave Boston. She returned to me about three months ago and asked me to begin the treatment again. The patient had a severe head cold, and the ear that had been dry was discharging once more. On examination I found both ears

suppurating freely. She could only come to Boston once a week, and I explained to her that I feared she would not get the same relief as when she came twice a week. She requested that I should try, and see if there would be any result. I have seen her now twelve times. The ears still discharge, but not nearly so much. She has gained over 10 pounds in weight. She gets more local reaction than she did formerly.

The injections have always been given in the arm, alternately on the left and right, in order to give the site of the injection the longest possible time to recover from any soreness. The skin of the arm where the vaccine is to be injected is well scrubbed with absolute alcohol. The glass hypodermic syringe is sterilized and the vaccine drawn into it under aseptic conditions. The injection is made in the upper arm, just above the elbow and close to the skin. After the first, and sometimes the second, dose of vaccine the patients complain of malaise, of a slight headache, and in a few instances of nausea. They also mention a feeling of depression. This is followed in about twelve hours by a sense of exhilaration which lasts about two and one-half days, and is followed by a slight depression. The injection is timed so as to come as the sense of exhilaration is wearing off and the depression is appearing. Most of the patients themselves noticed their improved physical condition while under the vaccine treatment. None of the patients lost weight while under this treatment; most of them gained, and their physical endurance was increased. So far I have not observed any complications or ill effects from vaccine.

It may be of interest to mention the different types of cases in which I have used this treatment. Chronic suppurative ears interest me especially, as they respond so readily to vaccine therapy. One of the ear cases had a large gland under the ear, which subsided rapidly under vaccine, and led me to the use of this agent in some cases of adenitis. I am not yet in a position to make a definite statement as to the results, but I feel that they are favorable. My success in treating nasal cases with vaccine is not, I regret to say, to be compared with that I have obtained in discharging ears. Whether it is due to the type of bacteria which one finds in the nose or to the preparation of the vaccine I do not know. The bacteria in the nose are not virulent, as a rule, and they probably owe their altered conditions and their lack of virulency to the antiseptic secretion in the nose. I have repeatedly taken cultures from the noses of patients suffering from atrophic rhinitis, and have always secured a pure culture of a short bacillus, which I have not identified yet. I have made a vaccine from this organism and injected it into patients suffering from this disease. There is a marked improvement in regard to crusts and odor. In patients who have had large crusts in the nose there is present after vaccine treatment only a slight amount of mucus, but no crusts. The odor disappears. These patients have greatly improved; but to keep them in that condition the vaccine treatment must be continued. I tried 2 atrophic rhinitis patients with staphylococcus vaccine for several months, but they improved only slightly. I am still carrying on investigations in this method of treatment, but it must be remembered that this is a new field and progress is necessarily slow.

DISCUSSION.

Dr. F. E. Stewart, Philadelphia: I would like to ascertain from Dr. Nagle what bacteria are generally present? The doctor referred to the streptococcus and staphylococcus. Are those germs usually present? Does the doctor find mixed infection in most cases? In regard to the various methods for killing the bacteria in preparing bacterial vaccines there is a great deal of difference of opinion. Some use phenol, and others, heat. Those who employ phenol believe that heat injures the product, while the others believe that phenol, on account of its action on albuminous matter, injures the product more than heat. In regard to containers, some Boston physicians use a vial of about 20-c.c. capacity and employ a rubber nipple without a hole in it for a cap. This kind of nipple is known as a "pacifier." After the vaccine is prepared and placed in the container the latter is capped with the nipple and, if heat is used for killing the bacteria, the whole is plunged into hot water and the heat maintained at about 60° C. for an hour. When the physician wishes to obtain a dose of vaccine he plunges the hypodermic needle through the nipple and withdraws the proper amount for injection. The needle hole immediately seals itself when the needle is withdrawn from the rubber. Manufacturers of bacterial vaccines use 20-c.c. vials with rubber caps, which accomplish the same purpose.

Dr. J. Blake White, New York: As a matter which might appear of importance in all methods of treatment, I desire to ask whether the doctor carried out any other method or line of treatment in addition to the vaccine therapy described. Such might modify, in some degree, the value of the vaccine effect as a curative measure *per se.* The report of the cases is certainly interesting and introduces a field for further investigation and experience which can be followed to advantage.

Dr. Nagle: The bacteria found in the ear were in most of the cases the staphylococcus, the streptococcus, and, besides, a great number of bacteria which it was impossible to identify. In the nose cases also I found a great many different kinds beside the staphylococcus and streptococcus. In the nose and throat, bacteria are so modified that it is very hard to identify them. I am working with these bacteria at the present time, trying to classify them and to find out more about them. I use the nipple arrangement for sealing vaccine bottles because it seems to be a very easy one. Although many contend that one is apt to get infections by this method, I have never had a single case of infection, though I have given a great many injections. The line of treatment that I use while giving the vaccine is just simply a cleansing method. The cases that I reported were all chronic discharging ears on which all the usual methods of treatment had been carried out previous to the vaccine treatment. I employed no general treatment whatever.

DIOXYDIAMIDOARSENOBENZOL AS A PATENTED PRODUCT.

By F. E. STEWART, Ph.G., M.D.,
GERMANTOWN, PA.

We are told that Ehrlich made an arrangement with the German chemical house of Meister, Lucius & Brüning whereby said house furnished him with the money necessary to carry on the 606 experiments which resulted in his discovery of dioxydiamidoarsenobenzol, with the understanding that if a product were obtained of sufficient value to warrant its commercial introduction it was to be patented and the patent controlled by the commercial house mentioned.

Position of Germany in Relation to Materia Medica Product Patents.

The arrangement that Ehrlich has made with Meister, Lucius & Brüning must be considered in the light of the German patent law, which excepts from patent protection: "(1) inventions the application of which is contrary to the laws or public morals; (2) inventions relating to articles of food, whether for nourishment or for enjoyment, and medicines, as also substances prepared by chemical processes in so far as the inventions do not relate to a definite process for the preparation thereof."

Patents are granted, however, for processes and apparatus for manufacture, and Section 35 provides a method for protecting the inventors of processes for preparing new products in the following manner: "If the invention relates to a process for the production of a new substance, all substances of like nature are considered as having been made by the patented process until proof to the contrary is given."

Materia Medica Products Exempt from Patent Protection in Most Foreign Countries.

Medicines are excluded from patent protection not only in Germany, but also in France, Austria-Hungary, Italy, Japan, Denmark, Norway, Sweden, Portugal, Russia, and a number of other countries.

Other classes of inventions excluded from protection in many countries, as well as Germany, are foods, chemical products, and inventions relating to war material.

Process Patents for Medicines Generally Allowed in Foreign Countries.

In all of these countries exclusion from protection of inventions relating to medicines or foods does not generally extend to those relating to processes

or apparatus for their manufacture. In all foreign countries which exclude chemical products from protection, except Switzerland, inventions relating to chemical processes may be patented, and in nearly all such countries it is expressly provided by law that a patent for a chemical process by which a new chemical product is made shall in effect cover such product, unless it be shown that such product was made in fact by some other process. In other words, when a new product is discovered, and a process of manufacture is patented, no person is permitted to compete with the original patentee unless he is able to show that the process he is to employ for that purpose is not an infringement upon the patented process.

THE UNITED STATES ALLOWS BOTH PROCESS AND PRODUCT PATENTS.

Under the United States patent law no class of useful inventions is excluded from protection. Any person who has discovered a new product to be used either as food or as a medicine may patent the same, and thereby acquire a monopoly of its production for a period of seventeen years. Foreign manufacturers take advantage of the United States patent law and patent their products in the United States. The monopoly thus acquired enables them to obtain a high price for their patented products during the life of the monopoly. The profit thus secured is not used for the benefit of American industries, but is applied to building up the industries of foreign countries at the expense of the American people.

THE A. PH. A. AND N. A. R. D. PROTEST AGAINST PRODUCT PATENTS.

A commission was appointed under act of Congress, approved June 4, 1898, to "revise the statutes relating to patents, trade and other marks, and trade and commercial names." It was urged before this commission, both at its hearings and in written communications read before it, that the United States patent law should be amended to exclude from patent protection both medicines and chemical products generally, at least insofar as such inventions are the inventions of subjects or citizens of the foreign countries which exclude this class of inventions from patent protection, and it was contended then, and has been the contention ever since, that subjects or citizens of foreign countries should not be allowed to receive in this country patents for inventions which are not patentable in their own country.

CO-OPERATION BETWEEN PROFESSIONAL AND COMMERCIAL INTERESTS IS ETHICAL IN GERMANY, BUT NOT ETHICAL IN THE UNITED STATES BECAUSE OF PRODUCT PATENTS IN THE LATTER COUNTRY.

In spite of all the protests the American Pharmaceutical Association and the National Retail Druggists' Association have placed before Congress, the United States patent law has not been amended to protect the American people. Consequently, in considering the question before us, it must be clearly understood that what I have to say in condemnation of the patent

system in connection with Ehrlich's invention applies exclusively to the United States. While it may be perfectly ethical for German physicians to co-operate with Ehrlich and Meister, Lucius & Brüning in the method which they have chosen for introducing dioxydiamidoarsenobenzol in Germany, it is certainly not ethical for the medical profession of this country to co-operate with them in the methods taken for the introduction of the product in this country.

The Educational Machinery of the Medical Profession Should be Controlled by the Profession, not by Commercial Houses.

The Hippocratic oath imposes the obligation upon each member of the medical profession to report the results of his experience and observations in the practice of the healing art to the common fund of knowledge, that his fellow-members may have the benefit of his inventions and discoveries. The proper introduction of new materia medica products requires the use of the educational machinery of the profession, *i.e.*, the professional press, societies, colleges, textbooks, pharmacopeias, and dispensatories. It is, therefore, essential that the profession shall have the control of this educational machinery to prevent the danger of commercial exploitation and the teaching of error, and shall not allow that control to pass into the hands of commercial houses engaged in the materia medica supply business. Because this fact has been lost sight of, and the control of the practice of the pharmacological arts has passed out of the hands of the medical profession and become vested in commercial houses presided over by business men who are not familiar with professional obligations, and who are engaged in introducing new materia medica products to commerce by advertising, that portion of the medical press accepting advertisements is placed in the position where it is attempting to simultaneously carry on a professional propaganda in the reading pages and a commercial propaganda in the advertising pages concerning the same materia medica products.

For a proper understanding of the question before us, it is necessary to consider the question of copyright itself.

The Question of Copyright, or the Right to Copy Writings and Inventions.

The question of copyright, which includes that of patent, is one of the most important subjects relating to man under the control of a civil government. The arguments for and against copyright were fought out in the so-called "Copyright War," which occurred in England about a century ago. The position taken by Lord Camden in opposition to copyright so well expresses the position of scientists generally in relation to patents that it is worthy of consideration at this time. In his speech Lord Camden said:—

> Glory is the reward of science, and those who deserve it scorn all meaner views. I speak not of the scribblers for bread, who tease the press with their wretched productions. Fourteen years are too long a period for their perishable trash. It was not for gain that Bacon, Newton, Milton, and Locke instructed and delighted the world. When the bookseller offered Milton five pounds for his Paradise Lost, he did not reject

it and commit his poem to the flames, nor did he accept the miserable pittance as the reward of his labor; he knew that the real price of his work was immortality and that posterity would pay it.

The position of his opponents is well illustrated by the following quotation from Terril in his treatise on patent laws:—

The theory upon which these laws rest is that it is to the interest of the community that persons should be induced to devote their time, energies, and resources to original investigation for the furtherance of science, the arts, and manufactures. This was recognized from the earliest periods which can pretend to be described as civilized. It is to the advantage of the whole community that authors and inventors should be rewarded, and no measure of reward can be conceived more just and equitable and bearing a closer relation to the benefit conferred by the particular individual than to grant him the sole right to his writing or discovery for a limited period of time.

In spite of Lord Camden and his brilliant speech, copyright legislation was successfully introduced in England, and I doubt whether the glory of Bacon, Newton, Milton, and Locke would have been dimmed in the least if they had copyrighted their books and made arrangements with publishers for a share of the profits from their sales. And, in spite of the opposition of the medical profession, the patenting of materia medica inventions will probably continue, and it is possible that the time will come when physicians will consider the patenting of inventions just as ethical as the copyrighting of books.

DIFFERENCE BETWEEN PRODUCTS AND BRANDS.

Ehrlich in patenting his product has brought the profession face to face with problems that must be solved, or there will be a day of reckoning in which the profession will be called upon by the public to give an account of its stewardship of the materia medica. For the license to practise medicine carries with it certain obligations on our part as physicians in relation to the materia medica, and to the arts of selecting, preparing, preserving, compounding, and dispensing medicines, that we cannot neglect with impunity. The science of materia medica is a part of medical science, and the pharmacological arts are just as much a part of medical practice as the art of therapeutics.

The first point to consider is the difference between products and names of products, and brands and names of brands, as illustrated by Ehrlich's product and the two names for it now in use,—dioxydiamidoarsenobenzol and the coined name under which it also appears. The latter is claimed as a trade-name or trade-mark by the commercial introducer. To understand the significance of this claim we must get a closer conception between products and names of products and brands and names of brands.

Condensed milk is the name of a product, and "Eagle" Brand, "Anglo-Swiss" Brand, and "White Cross" Brand are names of brands. Trichlormethane is a product. The name is long and unwieldy, so a short, euphonious name was coined for it, viz., "chloroform." But the name "chloroform" is just as much the name of a product as trichlormethane; and when the product is ordered by one name, the dispenser is justified in dispensing the product under either name. Is it not true that the coined name under which Ehrlich's

product is now offered is just as much the name of dioxydiamidoarsenobenzol as "chloroform" is the name of trichlormethane? Hexamethylenamine is the official name of a product. On turning to the National Dispensatory and other textbooks it will be noted that various synonyms are given for this. Each of these synonyms is claimed by the manufacturer as a trade-name or trade-mark. The question arises, Are druggists justified in purchasing hexamethylenamine under that name and dispensing it in physicians' prescriptions when the product has been specified under one of the so-called trade-names? Ask the several manufacturers who claim these names as trade-marks, and they will answer that druggists who purchase the product under the name hexamethylenamine and dispense it when it is prescribed under any one of the trade-names are guilty of fraudulent substitution. If the so-called trade-names are, in fact, brand names, manufacturers are right, and the textbooks are teaching fraudulent substitution. Conversely, if the textbooks are right, the manufacturers are wrong. Thus we have three kinds of claims relating to names, two of which are unwarranted and represent a serious abuse of the trade-mark system, and one of which is not only legitimate, but highly commendable, and represents the trade-mark system as properly applied in commerce.

Claims of the So-called Proprietary Medicine Trade.

Let us consider first the trade-mark abuse in which the names of unpatented medicines are claimed as the private property of the introducers. The claim is based on two other claims, the first being that unpublished formulas or methods of manufacture are trade secrets, and, therefore, the property of the manufacturers, and the second, that the names, being coined, are, therefore, the property of the inventors thereof. These are the claims of the so-called "proprietary" medicine manufacturers. They are erroneous. It has been decided by the courts again and again that any person who discovers a trade secret by legitimate means has a right to use it. When a secret is divulged, it is a trade secret no longer. As pointed out by the court in the celebrated Angostura Bitters case, while the medicine is monopolized the name of the product and the name of the brand are one and the same. But when the secret is divulged, the question arises whether the name is that of the product or the name of the brand, and the court decided that the name Angostura Bitters is the name of the product, on the ground that, the secret having been divulged, any person had an equal right to manufacture and deal in it. The same point came up incidentally in the decision of the U. S. Supreme Court in the Miles Medical Company case, in which attention was called to the fact that any person has the right to make and sell unpatented medicines if they know how to make them and have obtained their knowledge legitimately.

Coined Names are not Property because of Invention.

It is commonly believed that when a person coins or invents a name he possesses a natural right to its exclusive use because it is a "child of his brain." This, however, is an error. Authors and inventors do not possess a natural

right to prevent others copying their respective writings and discoveries. Copyright and patent-right are grants, not natural rights.

NAMES CANNOT BE COPYRIGHTED.

Many believe that invented names may be patented or copyrighted. This is also an error. As stated in Circular No. 19, issued by the Librarian of Congress, "the copyright laws contain no provision under which protection can be obtained upon a *mere name or title.* Entry cannot, therefore, be made in the copyright office for coined names; names of articles of manufacture; names of games or puzzles; names of substances; names of products, or names of medicines."

ATTEMPT TO DEFEAT THE OBJECT OF THE PATENT LAW.

The manufacturers of antipyrin, acetphenetidin, and many other German synthetics patented their products under the chemical names, and registered the coined names as trade-marks. Now as the right to use a trade-mark is a natural right, and is protected by the common law,—a manufacturer having just as much right to use his commercial signature for the purpose of indicating the source of his product as he has to sign his name to a check,—that right does not expire like a patent. Consequently, the manufacturers hoped by this scheme to defeat the object of the patent law, which is to promote progress in science and useful arts by granting inventors the exclusive right to their inventions for limited times, in exchange for the publication of full knowledge thereof by the proper application for patent. However, "Uncle Sam" has something to say about this. He said it in the decision of the Supreme Court of the United States in 1895, in the Singer Sewing Machine case. The decision reads as follows:—

DECISION OF THE SUPREME COURT OF THE UNITED STATES.

The result, then, of the American, the English, and the French doctrine universally upheld is this, that where during the life of a monopoly created by a patent a name, whether it be arbitrary or be that of the inventor, has become, by his consent, either express or tacit, the identifying and generic name of the thing patented this name passes to the public with the cessation of the monopoly which the patent created. Where another avails himself of this public dedication to make the machine and use the generic designation, he can do so in all forms, with the fullest liberty, by affixing such name to the machine, by referring to it in advertisements, and by other means, subject, however, to the condition that the name must be so used as not to deprive others of their rights or to deceive the public, and therefore that the name must be accompanied with such indications that the thing manufactured is the work of the one making it as will unmistakably inform the public of the fact.

THE CASE OF THE ACTIVE PRINCIPLE OF SUPRARENAL GLAND.

The evil of this combined product-patent and registered-name abuse is clearly shown in the case of the active principle of suprarenal gland now under litigation. Von Fürth, Abel, and others had demonstrated many of the properties of the adrenal secretion and had published the methods of prepara-

tion of the derivatives of the active principle, while Oliver and Schaefer had worked out the physiological action of this substance and indicated its usefulness in medicine. These methods were improved upon by Takamine and Aldrich, who independently and about the same time first isolated the active principle itself. Takamine's work was published first, and he was granted a product patent. His formula, however, has never been substantiated, while that of Aldrich has been verified by chemists both in this country and abroad. Basing its claims upon this product patent, the manufacturing house which now controls it is attempting to maintain for seventeen years monopoly of all preparations of this active principle, and, as clearly demonstrated by the recent discussion on the subject in the *Journal of the American Medical Association*, the manufacturer is also endeavoring to establish monopoly of the name given it as a trade-mark. It is evident that such a scheme as this permits the inventor to appropriate for exclusive use all of the prior work of von Fürth, Abel, and others, to their discredit, as also that of Aldrich, and that it enables the manufacturer controlling the patent to use the educational machinery of the medical profession for commercial exploitation; also that it converts every textbook in which the name appears into a permanent advertisement for which the manufacturer pays nothing.

Why is it Ethical for the Medical Profession to Co-operate with Chemical Manufacturers in Germany and Not Ethical in the United States?

Physicians with whom I have talked on the subject ask why it is that the medical profession in Germany co-operates with commercial houses for the introduction of monopolized materia medica products. Germany is in the van in all matters scientific. Why should not the United States follow her lead? Take Ehrlich's invention, for example: It is patented in Germany, yet the public institutions of Germany are thrown open to its commercial introducers, and the leaders of the profession in Germany are foremost in attesting to its virtues in hospital and private practice and reporting the results. Ehrlich's invention occupies a very different position in Germany from that which it does in the United States. The German government granted Ehrlich the right to prevent others from manufacturing the product according to the process invented by him, but did not grant the right to prevent others from preparing the product by some other process. The product is not monopolized in Germany. Its status is similar to that of acetphenetidin before the patent for the Bayer process expired. Several brands of this product, made by different patented processes, were sold in competition with the brand prepared by the original process. But the United States government granted the inventor of the original process a right to prevent others from making acetphenetidin in this country; also the right to prevent the sale of the imported acetphenetidin, thus preventing competition and enabling the German manufacturers to charge $16.00 a pound for the product in the United States which it was selling for $3.00 or $4.00 elsewhere, and to build up a foreign industry at the expense of

the American people. It is probable that long before the German patent expires several other brands of dioxydiamidoarsenobenzol will appear on the market and be sold in Germany and other foreign countries at less than half the price that it will be sold for in this country. The reason why it is professional for German scientists to co-operate with German chemical houses, while it is unprofessional for American physicians to do so, is, therefore, apparent.

ACTION OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION.

The Council on Pharmacy and Chemistry of the American Medical Association attempted to remedy conditions pertaining to the case of the active principle of suprarenal gland by refusing to recognize the trade-name as generic, and substituting the name "epinephrin" in place of it. The Council has the power to do this in the Journal of the Association; but the dispensatories and other textbooks recognize the trade-name as the name of the product, and the government orders the product under that name in purchasing supplies. The controversy between the Journal and the manufacturer has had the very opposite effect from that really intended, as will be perceived on re-reading the decision of the Supreme Court in the Singer Sewing Machine case.

REMEDY IN THE HANDS OF THE MEDICAL AND PHARMACEUTICAL SOCIETIES.

It is the function of the medical societies to co-operate with the pharmaceutical societies and the committee having charge of the revision of the United States Pharmacopœia in settling questions of nomenclature. If the American Therapeutic Society should officially adopt the coined name as the name of Ehrlich's product,—and, therefore, synonymous with dioxydiamidoarsenobenzol,—and so notify the manufacturer, what would probably follow? If the manufacturer accepted the decision of the Society, no further doubt concerning the status of the name would exist. If the manufacturers protested, the medical journals which have given the manufacturer millions of dollars' worth of advertising without charge would have the opportunity of considering what to do about it. If the manufacturer ignored the Society in the matter, the decision of the Supreme Court would apply, to wit: "that where, during the life of a monopoly created by a patent, a name has become, by the inventor's consent, the identifying and generic name of the thing patented, this name passes to the public with the cessation of the monopoly which the patent created."

SIMILARITY BETWEEN PATENT GRANTS AND LICENSE TO PRACTISE MEDICINE AND PHARMACY.

There is a great similarity between patent grants and license to practise medicine and pharmacy. A patent grant includes the exclusive right to practise the invention. A license includes the exclusive right to practise medicine or

pharmacy. The patent grant is given in exchange for the publication of the invention. The license to practise is given in exchange for professional services. It is essential to the welfare of the community that the practice of medicine and pharmacy should be limited to qualified practitioners. For this reason, the license to practise is not granted to persons who are not educated as physicians or as pharmacists. Only such are qualified to render proper service to the public in caring for the sick and preparing medicine for that purpose.

The Nostrum Invasion.

During the past fifty years the United States and England have been suffering with a nostrum invasion. Now, a nostrum differs from a legitimate pharmaceutical preparation only because of the monopoly, secrecy and pretense surrounding it. Nostrums are often called "quack" medicines. Medicines cannot quack—the quacking is done by their alleged inventors. Pretense in advertising on labels, in circular matter, in medical and pharmaceutical journal advertisements, and in the newspapers, is the worst kind of quackery. It is this kind of commercial propaganda I object to. When the propaganda is designed to spread the false therapeutic doctrines of alleged inventors of so-called specifics or cures among the people at large, the evil is clearly recognized by the medical profession. Then it is known as the "great American fraud." But when the propaganda is designed to fool the medical profession, its dangers are not so apparent, for the methods employed are more insidious. To vest the control of medical and pharmaceutical practice in the hands of ignorant merchants and manufacturers, who are unable to appreciate the responsibilities involved and are engaged in conducting a propaganda for the dissemination of pretense and error, amounts to the same thing as licensing quacks to practise medicine and pharmacy. As our laws now stand, any person, no matter how ignorant or venal, can set up as a manufacturer and practise both professions at wholesale without hindrance, while the educated physicians and pharmacists are not permitted to practise without a special license from a board of examiners. The incongruity and absurdity of such laws require no comment.

The Patent and Trade-mark Laws Used to Protect the Nostrum Business.

As now administered, the patent and trade-mark laws are used by the nostrum trade to protect its nefarious business. This trade twists, contorts, and stretches the patent and trade-mark laws to hide its Satanic character. It fools its victims by false promises and fraudulent claims, and those engaged in the business not only deceive the medical profession and the public, but they actually fool themselves by their own sophistries, until they half believe their own lies and begin to imagine they are telling the truth. As there is no real distinction between a nostrum and a legitimate pharmaceutical preparation except as to the manner in which it is introduced, and as the manufacturers of synthetic chemicals intended for the medical profession, as well as the manu-

facturers of products intended for the lay public, both employ to a greater or less extent a commercial propaganda characterized by secrecy, monopoly and misleading advertisements, and also employ the patent and trade-mark laws to protect them in so doing, it is very necessary for the profession to draw a clear line of demarcation between the commercial propaganda of the nostrum business and the professional propaganda which should characterize honest chemical and pharmaceutical houses, and then insist that the manufacturers shall clean up their propaganda and keep it clean.

Protection to brands by process patents and brand names is necessary to public welfare, but the monopoly of materia medica products and the control of their currently used names is an abuse against which the medical nad pharmaceutical professions should strongly protest. If our process patent law is not sufficiently protective to brands, as some would have us believe, then let us so amend the law as to make it truly protective. It is folly for the manufacturers of monopolized products to say as did Boss Tweed, "What are you going to do about it?" If the medical and pharmaceutical professions unite and demand proper legislation, they will certainly obtain it. Furthermore, the Supreme Court has a perfect right to cancel any patent, as illustrated by the action of the Supreme Court in relation to Morse's patent. The patent covered the transmission of messages by electricity, and the court decided that such a patent was contrary to public welfare and refused to sustain it. Medicines are used for the healing of the sick, and the patenting of medicines, which enables manufacturers not only to charge exorbitant prices for them, but protects a commercial propaganda intended to deceive the medical profession and the public, is surely as inimical to public welfare as the patenting of such an invention as that of Morse.

It will thus be seen that the consideration of dioxydiamidoarsenobenzol as a patented product includes the greater question of patents, copyrights and trade-marks, as applied to medicine, and that this question involves a still greater question, and that is whether the medical and pharmaceutical professions are to permit dishonest manufacturers longer to invade the field of medical and pharmaceutical practice and use the professions to aid them in exploiting the sick-room for gain. We cannot endorse the Ehrlich product patent and the use of its coined name as a trade-mark without also endorsing the system of materia medica monopoly above described, for although Ehrlich and his commercial agents have apparently acted with perfect integrity, yet the system of protection they have adopted for the control of their product is contrary to public welfare.

SUMMARY AND REMARKS.

1. The object of the patent law being to promote progress in science and the useful arts, it logically follows that its proper application to materia medica inventions will promote progress in materia medica science and the arts of preparing medicine and applying the same to the healing of the sick. As now applied, the patent law hinders progress in the knowledge of drugs as therapeutic agents and injures the professions of medicine and pharmacy.

2. Product patents are monopolies granted to persons who are not required to be interested in promoting science or in advancing the arts of medicine and pharmacy. Their object is, not to conduct a professional business to promote the interests of the medical and pharmaceutical professions and conserve the public welfare, but to conduct a commercial business to make money.

3. Progress in materia medica science, and in the pharmacological arts, is dependent upon the co-operation of those engaged in the practice of the pharmacological arts and in the results of the publication of their researches for the benefit of science. Investigations in many branches of science are necessary to develop knowledge of new medicinal drugs and chemicals. Chemistry, physics, botany, bacteriology, biology, physiology, pharmacy, pharmacotherapy —all must be drawn upon. And all who are engaged in the work of development must obtain a living directly or indirectly from materia medica commerce unless they are employed in the laboratories of educational institutions or of the government.

4. The position assumed by certain members of the medical profession that it is immoral for physicians to make money out of the sale of drugs is unwarranted. If I am wrong about this, how about the editors and publishers of medical journals who derive an income from the advertising patronage of commercial houses engaged in the materia medica supply business? No, the wrong is not in making money. The wrong is in carrying on what ought to be a professional business in a commercial manner. This becomes at once apparent when it is considered that physicians are dependent upon the knowledge thus involved for treating the sick—and dependent upon this science, therefore, are the Pharmacopeia, medical and pharmaceutical textbooks, and the schools and colleges teaching medicine and pharmacy.

5. Materia medica products cannot be properly introduced to science without using the educational machinery of the profession, viz., medical societies and press. When the product is controlled by commercial introducers, their introduction to science by the co-operative work of the profession is impracticable, because the opening of the journals and medical societies to their discussion converts the educational machinery of the profession into a great advertising bureau for the exploitation of monopoly.

6. Most of the experimental work necessary for determining the therapeutic value of new therapeutic agents is carried on in hospitals, dispensaries, asylums and other charitable institutions. The right to use the sick for experimental purposes is one of the highest privileges vouchsafed the medical profession. Only for humanitarian purposes, that all may benefit, are such experiments justified. When the results are appropriated by commercial houses for building up materia medica monopolies, beneficence is turned into commercial exploitation. The exploitation of the sick for gain is a crime against humanity that humanity will punish sooner or later, when the people appreciate the situation.

7. Under a system of competition it is safe to open the educational institutions and their laboratories to the manufacturers of materia medica products and ask their co-operation in developing the science of materia medica.

There is no danger by so doing that the educational machinery of the profession will be converted into a great advertising bureau for the commercial exploitation of monopolized products. The burden of expense is shared between the colleges, universities and medical press, and the commercial introducers of brands. The artificial character of the demand resulting alike from the publications of both scientific and commercial introducers is corrected by impartial discussions in medical societies and journals. Brands are advertised in the advertising pages of the medical journals without endangering the integrity of the reading pages, and the more brands advertised the less the danger. One of the results is a largely increasing demand for all new products of therapeutic value from which the manufacturers of brands obtain their share of the profit without the outlay of the enormous amount of capital required for introducing new monopolized materia medica products by advertising.

8. Under the system of product patents maintained in this country the medical journals are forced to give the manufacturers advertising space that millions of money could not purchase. They have been forced to do it to keep pace with the foreign journals in publishing important news. They have aided the manufacturer in building up a monopoly in this country because of our product patent system. Foreign journals, in countries where product patents are not allowed, have kept their skirts clear. Except for the product patent, there would be an opening for more than one brand and more than one advertiser. Therefore, as a business proposition, the propaganda adopted for the introduction of new materia medica products in the United States is not a good one, at least for the medical journals.

In conclusion, I believe that the arrangement made by Ehrlich with the German chemical house, Meister, Lucius & Brüning, represents a plan of co-operation between professional and commercial interests, which, if purged of the monopolistic feature now pertaining to it, might be made in every way commendable. The great manufacturing houses engaged in the chemical and pharmacal industries, with their scientific departments, are in a position to render the most valuable kind of service to the medical profession. They possess large capital, large facilities, and enormous influence. They are provided with scientific departments, including men of national and international reputation as chemists, physiologists, pharmacists, bacteriologists and physicians. Co-operation between the medical profession and the manufacturing houses engaged in the materia medica supply business would do more than any one thing to promote progress in the science of medicine and the useful arts of preparing materia medica products and applying them to the treatment of the sick. But such co-operation must include control of the practice of the pharmacological arts by licensed practitioners of medicine and pharmacy, and compliance with rules for the advancement of pharmacological science. Medicine, including pharmacy, is an altruistic profession. Its object is to prevent disease and heal the sick, not to exploit the sick-room for gain. Co-operation between the medical and pharmaceutical professions and the great manufacturing houses with that end in view spells progress.

DISCUSSION.

Dr. Thomas E. Satterthwaite, New York: This is an important question, it seems to me, and I think it would be well for the Society to learn the relation between ourselves and the pharmaceutical bodies in respect to certain drugs. There is no doubt that many of the great manufacturing houses are doing good work, and there is no reason why we should not in some way be in touch with them. I propose to make the following motion before the Council:—

Resolved, That a Committee on Nomenclature, composed of three members, be appointed by the President, for the purpose of conferring with the American Pharmaceutical Association and other scientific bodies interested in fixing the terminology of the newer materia medica product; the same to report at the next annual meeting of the American Therapeutic Society.

Dr. H. C. Gordinier, Troy, N. Y.: It seems to me that the resolution which Dr. Satterthwaite is to bring before the Council is most important; I certainly feel in favor of what it stands for.

Dr. Spencer L. Dawes, Albany, N. Y.: I want to register my approval of the position of Dr. Stewart. In order to avoid the use of trade names we have incorporated into our pharmaceutical vocabulary such names as hexamethylenamina and sulphonethylmethanum, in place of simple, ordinary names that we are all familiar with and which we all of us use, and it seems to me that we are simply extending a condition that we are trying to get out of. I think it is time that the so-called learned societies get together and find a way out of this situation.

ON THE USES OF NICKEL SULPHATE IN MEDICINE.

By LOUIS KOLIPINSKI, M.D.,

WASHINGTON, D. C.

SUFFICIENT proof has made it evident that nickel salts are useful in practical medicine, and that they may aid or supplant other remedies now in vogue, yielding equal or better results. Until this time, however, the nickel salts, commended by different writers after successful use, have remained in obscurity; nor have the original observations concerning them so far been verified or extended. It is the purpose of this article to review the medical history of nickel, and to add thereto what has thus far been found out concerning it in personal practice.

All experimenters agree that acute or chronic poisoning does not result from the use of nickel implements, instruments, and vessels used in the arts or in domestic cooking. F. Geerkens,[1] Laborde and Riche,[2] Rohde,[3] and van Haniel Roos[4] have declared this opinion, which, further, is in full accord with the non-poisonous action of nickel when fed to animals in a natural way. Large daily doses greatly improve nutrition in the dog, acting, as stated by Simpson, as a gentle metallic tonic. Nickel and nickel salts therefore, excepting the very poisonous nickel carbonyl, have no place or record in toxicology. The case of the Emperor of Austria, Francis Joseph, where an illness was supposed to be due to the use of nickel cooking-vessels, is doubtful, and against the belief of the writers just quoted. The only other case in medical literature is that of Dr. George Richter.[5] A polisher of aluminum, copper, brass, and more particularly of nickel was supposed to have been poisoned, because it seemed plausible that a certain amount of metallic nickel dust had accumulated in the bowels, and that some of it had passed through the intestinal walls or been dissolved by the action of the hydrochloric acid of the stomach. Richter failed to prove any nickel elimination in the urine with the spectroscope. The clinical symptoms were indefinite.

T. P. Anderson Stuart[6] found that in the frog nickel, in its general action, causes darkening of the skin. The animal remains quiet and weak, with twitching of the muscles in progression and cramps. There are true tetanic attacks, like those in strychnine poisoning. Stupefaction sets in after voluntary motor paresis. After paralysis of respiration the heart ceases to

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1 "Experiment. Untersuch. über die Wirkungen von Nickelsalzen," Inaug. Dissert., Bonn, 1883.

2 Tribune Médicale, xx, 1888.

3 Arch. f. Hyg., ix, 1889, p. 331.

4 Internat. Cong. f. Hygien. und Demograph., vi, 1887-8.

5 Jour. Amer. Med. Assoc., vol. xlix, 1907.

6 Jour. Anat. and Physiol., London, 1882-3.

beat. On the striped muscle there is no effect. As regards the nervous system, the paralysis involves to some extent the cerebrum and is preceded by exaltation. Nickel does not seriously affect the motor ganglia of the heart. There is no change in the red blood-corpuscles.

In the pigeon, rat, and guinea-pig there occur stupor, feeble voluntary movements, and unsteadiness, and death ensues quietly. In the rabbit there occur rapid pulse and respiration, and paralysis of the hind- or fore- legs, or both; also persistent diarrhea. If the paralysis disappears after a dose not speedily fatal, there is a stage of excitement with twitchings and contractions, slow and difficult respiration, dilated fundi oculi and ear vessels, and convulsions ending in a fatal one. The heart continues to beat some minutes after the breathing stops. *Post mortem* extravasated blood is found in the gastric and intestinal mucosæ, with ulcers in the stomach. On the intestinal mucous membrane the action is less destructive. The tonic and clonic spasms and nervous symptoms in animals are spinal, and not due to the stage of asphyxia.

In dogs and cats motor excitement does not appear when nickel solution is injected into a vein slowly or when the injection is made subcutaneously. The animal lies exhausted; heart-action is rapid and strong; respiration, rapid and deep. There are myosis, vomiting from the beginning, and convulsions followed by complete voluntary motor paralysis. With the convulsions there is failure of the respiration, the heart-action continuing. In subacute or chronic poisoning the vomiting continues. There are also serous diarrhea, stomatitis, bad odor of the mouth, softening of the gums, eructation of ill-smelling gases, black feces. Epileptiform convulsions occur. The urine remains of normal color, unlike the case in cobalt. Death results, as in an acute case. The respiratory changes are due to excitation and paralysis of the centers in the medulla. In the rabbit, dog, and cat the arterial blood-pressure falls continuously till death, if the dose is large. This fall is due to a specific action on the vasomotor center in the medulla, and not to any action of nickel on the heart. The pulse increases, then decreases, without specific cause. Nickel and cobalt resemble arsenic in their action on the vascular system, the alimentary tract, and, to a certain extent, in the effect on the nervous system. Nickel is absorbed when the solution is painted on the skin of the frog. It is difficult to produce death in animals from poisonous doses of nickel introduced into the stomach. Nickel is excreted chiefly with the urine, but also in the bile and feces.

Franz Geerkens[7] found, as stated, the economic use of nickel-plated vessels harmless. He observed that in the rabbit 1 Gm. of nickel acetate, introduced into the stomach, is fatal. In the dog 0.5 Gm. of the acetate has no harmful effect, and 14.5 Gm. in the same animal in four weeks increase the weight. 0.4 Gm. injected into a rabbit's vein is fatal, with symptoms and pathological changes like those of arsenic or corrosive sublimate.

In frogs death results from cardiac paralysis. Nickel salts are antiseptic, the most active in this respect being the chloride.

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[7] *Loc. cit.*

Laborde and Riche[8] state, as the results of animal experiments to determine the physiological action of nickel salts, that a poisonous effect on animals is obtainable only by hypodermic and intravenous injection in the ratio 0.5 to 1.0 Gm. per kg. of the animal. There appear convulsions and tetanic contracture, vomiting and diarrhea, paralytic collapse, and lethal asphyxia. There are enfeebled heart-action and diminished blood-pressure. Nickel produces vomiting and cardiopulmonary disturbance by acting on the bulbar centers. In the stomach of a dog 0.5 to 3 Gm. of a nickel salt produce vomiting and diarrhea, a fall of temperature, feebleness, and stupor, but not death. Nickel is less poisonous than copper.

H. A. Hare[9] believes that the action of the bromide of nickel on animals is to affect the spinal cord and its afferent and efferent nerves, and to paralyze the contractile power of the heart muscle, which stops in diastole. This is true of the frog and of higher animals as well. The fall of blood-pressure is due to cardiac failure and to vasomotor paralysis. Small and large doses momentarily slow the heart.

Henri Coupin[10] finds nickel and cobalt poisonous to higher vegetation. On germinating wheat nickel chloride and sulphate are very toxic, with equivalents of 0.020 and 0.022. The cobalt salts are slightly less destructive.

Since nickel acetate causes fatal poisoning in a dog when used hypodermically, setting up a grave gastroenteritis such as results also from arsenic and corrosive sublimate, H. Schulz,[11] theoretically, presumed nickel salts to be antiseptic. He selected the chloride for his experiments. He found it preserved fibrin and defibrinated blood, 1.0 Gm. to the liter. Aspergillus glaucus growth on bread was restrained or diminished by it. It was fatal to paramecium grown in decaying hay infusion. Schulz thinks this nickel salt acts by absorbing ammonia and liberating chlorine on atmospheric contact. He recommends it in practice in place of corrosive sublimate.

E. Manoilow[12] finds the effect of nickel salts on micro-organisms to be less poisonous than that of copper and other metals, though its action varies in the case of different microbes. The neutral nickel salt of Heldt inhibits the growth of the bacillus of typhoid, of the bacillus pyocyaneus of osteomyelitis, of the staphylococcus, and of the cholera vibrio. Proportionate strength, 0.003 Gm. to 1 c.c. It also inhibits the growth of the following: The bacillus coli communis, in the strength of 0.0095 Gm. to 1 c.c.; aspergillus flavus, aspergillus niger, and mucor corymbifer, 0.0046, 0.0095 Gm. to 1 c.c. (kills in the strength of 0.016-0.019 Gm. to 1 c.c.); saccharomyces cerevisiæ et roseus (ruber), 0.00895 Gm. to 1 c.c. (kills, 0.017-0.710 to 1 c.c.); bacillus prodigiosus and bacillus subtilis, 0.0058-0.007 (kills, 0.0196-0.0122).

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8 *Loc. cit.*

9 Therapeutic Gazette, Detroit, Mich., 1886, x, 3 S., 2.

10 Compt. Rend. Hebdom. des Séances et Mém. de la Soc. de biol., Paris, 1901, tome iii, ii Sr.

11 Deut. med. Wochenschr., viii, 1882.

12 Centralbl. für Bakteriol. u. Parasitenkunde, 2 Abt., 1907, p. 18.

In practical medicine, the following are the putative uses made of nickel in the last century: J. Y. Simpson[13] first administered nickel in practice. He held the sulphate to be a gentle metallic tonic. The dose was ½ to 1 grain after meals. Its action was like that of manganese or iron. He found it useful in periodic headache, chlorosis, and amenorrhea.

J. Dabney Palmer,[14] because of Simpson's successful case of obstinate periodic headache, gave nickel sulphate to a lady suffering with severe facial neuralgia. It acted as a sedative like potassium bromide, reducing the pulse and producing sleep, and gave more permanent relief than anything else. A considerable number of drugs had been tried before. The patient said it soothed more quickly than morphine.

J. M. Da Costa[15] states that the best nickel salts are the sulphate and bromide. The sulphate may be given in doses of 1 to 3 grains. Five grains in some cause nausea and giddiness. The larger doses reduce the pulse and lower temperature. It has no soporific effect, but is something of an anodyne. No proof was seen of its tonic effect. Excellent results were produced in obstinate diarrhea. Both the chloride and the sulphate have a calming influence on the nervous system. Compressed tablets of nickel bromide do not keep well. This salt has the effects of the other bromides, but in much smaller doses—5 to 7½ grains an average, 10 grains a decided, dose. It is best to give 5 grains, soon repeated, this being less liable to disturb the stomach. Its influence on the nervous system is shown by the relief of headache, especially of the congestive form, and in its effect on convulsive movements and its general quieting tendencies. In epilepsy very favorable results were obtained from the bromide of nickel, but less striking effects from the chloride or sulphate.

R. Leaman[16] found that the bromide of nickel, 5 to 10 grains, gives the best results in epilepsy with regular, but not frequent attacks, where the object in view is to keep up a mild impression for a long while. It disorders the digestion less than any other bromide, especially when administered in the effervescing form.

In the following results of treatment of a variety of diseases the sulphate was the salt of nickel chosen as being more suitable to determine any primary therapeutic actions inherent in this metal than other compounds of it, such as the iodide, bromide, or chloride. Good results were obtained, confirming in some instances the statements of former practitioners, in others modifying or amplifying them. In still others new remedial virtues were discovered.

The dose of nickel sulphate is 1 grain, after meals or food, three or four times a day. One-half grain will often achieve good therapeutic action, but the larger dose is surer and as well borne. Two to 5 grains or more are so prone to cause severe nausea and vomiting that these quantities must be

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13 Contrib. Obstet. Path., Edin., 1853, p. 37.

14 Richmond and Louisville Medical Journal, vol. v-vi, 1868, p. 270.

15 Medical News, Philadelphia, xliii, p. 337, 1883.

16 *Ibid.*, xlvi, 1885.

considered too large for practical use. The forms of administration are pill, tablet, and solution.

Nickel and cobalt, though closely related chemically and physically and similar in toxic action, are widely different as germicides, and, as medicinal agents, nickel is active and variedly useful, while cobalt is apparently inert. Nickel sulphate was found to be potent as a germ-destroyer and as an antiseptic, in the proportion of 1 to 1900. As a result of the noting of its active bactericidal power, it was applied in several of the commoner parasitic skin diseases with success. Arrest of evolution and healing of the lesions resulted when it was applied in aqueous solution, in a strength of 1 to 2 per cent. It can be used as a wet compress, or mopped or brushed on the skin and allowed to dry there. It was found to cure impetigo contagiosa, pityriasis versicolor or chromophytosis, trichophytosis corporis or ringworm of the body, and that other more obstinate form of eruption to treat, eczema marginatum. Alopecia areata showed a faint growth of very fine new hair at the end of a week, and at the end of six weeks normal scalp and hair covering. In acne vulgaris it is a good remedy applied locally several times a day, and where the subject is young and pale, as is commonly the case in this disease, it may also at the same time be given internally.

Nickel sulphate is of considerable benefit when given internally in some other skin diseases also. Thus, in chronic urticaria due to heart weakness and the exhaustion of daily labor or exertion, it gives relief from the breaking out of the eruption prone to occur nightly, with its torment of itching. It abates the same sense of irritation and the burning in erythema exudativum multiforme, thereby inducing rest and sleep. In chronic psoriasis it acts well, in place of arsenic, to hold in check the tendency to recurrence and the spread of the existing disease.

In chorea a cure can be accomplished in three or four weeks. The patient's nutrition is much improved, and the figure becomes more robust. Nickel seems to be fully the equal of arsenic in efficiency, and has none of the disagreeable disturbances of mild arsenicalism, such as edema, headache, nausea, or vomiting. It has also been found to act well in this disease in cases where arsenic had first been used to the border line of tolerance and its discontinuance become a necessity. The nickel salt in such instances seems to cure even more speedily.

Nickel will also be found a new and useful remedy in a motor disturbance with spasm and inco-ordination much unlike the last, and one in which the use of medicinal remedies is almost an untried power. In stammering in children and adults the speech is very much improved after the sulphate has been taken for two or three months. The nutrition and vigor of the subject are markedly improved, and his manner loses its timidity and becomes confident. As in chorea, arsenic is also useful in this defect of speech, but nickel will be found preferable.

In chronic neuralgia of the face, tic douloureux, it has been successfully given, confirming the observations of J. Dabney Palmer. Among them was one of a middle-aged woman with right inferior dental neuralgia in whom

nerve resection had been done eight years before, with relief for a year or more. The patient had been previously treated with potassium iodide, and then with pyroligneous acid, both drugs being successful for some months and then failing absolutely to relieve her. One grain of nickel sulphate four times a day gave much ease for some time. In another case of inferior dental neuralgia in an old lady, who had suffered for about twelve years, alcohol injections, repeated several times, stopped the pain for some months. The neuralgia then returned with increased violence, and, in despair of relief, she refused to submit to another injection. The patient had a fairly developed arthritis deformans in the knee and shoulder joints. Pyroligneous acid speedily removed the stiffness and pain of the articulations, and also abolished the daily paroxysms of tic douloureux. The remedy was then discontinued, and the neuralgia remained absent for four months. Afterward, as the pyroligneous acid was an unpalatable draught to her, nickel sulphate was substituted, and its effect in abolishing the pain was prompt.

In migraine of whatever form, nickel is one of the best and most efficient means of treatment. In middle-aged females of consumptive ancestry who have had this variety of headache for twenty years and more—a class that affords the most frequent and severe examples of hemicrania—this remedy has been found to cure. Migraine is probably a gastric or intestinal toxemia from food which is beyond the patient's digestive power. The nickel salt prevents this outburst of poisoning by its direct antiseptic and antitoxic action. The experience had with it in the preventive treatment of this disease confirms that of Simpson in a case of periodic headache narrated by him.

In chronic enteritis the sulphate was found to be a good remedy, but, as with others, subservient to diet. It has also been found to prevent relapse in consequence of a promiscuous diet in tuberculous and other chronic diarrheas after cure. All this is confirmatory of the results reported by Da Costa in a case of obstinate diarrhea.

In epilepsy the sulphate has not been found curative or preventive of seizures. Where the epileptic fits were periodic and infrequent, they reappeared with customary force and regularity. As nickel bromide was not included in the scope of this test, its action in this malady was not sought for. Yet it cannot be stated as absolutely true that nickel is without any positive effects in suppressing the epileptic seizure, for in a case where the sulphate had been exhibited without result for several months the epilepsy was suppressed under its continued use when reinforced with a single dose of sodium bromide given at bedtime. In view of this result it can be assumed that nickel may yet be of value as an adjuvant to the much more potent bromides, especially as a much reduced dose of the latter is required when this is employed. Further, the nickel assumes a more important place in the treatment of this afflicting disease in cases where its origin or existence is associated with inaction or perversion of the genital sphere and organs.

It was noted that nickel is of important service in the treatment of the emotional and psychic weakness, the vague ideation, and the instability of character and action met with in celibates of both sexes—the marked defi-

ciency in vigor of mind and the enfeeblement of energy and will, the singularity of conduct, the shyness in manner, the tendency to seek retirement, the morbid affections, and the various other traits that make the confirmed bachelor and the real old maid subjects of levity or contempt. Such persons are sad and tearful, suffer from loss of memory and sleeplessness, are nervous, irritable, dyspeptic, and constipated, and often have a morbid belief in the presence of some non-existent disease.

They are classed as neurasthenic. There is enfeeblement of vital power from prolonged sexual continence, and the suffering in this undefined way, with the constant unrest, alters the individual character and impairs the health. The sulphate of nickel relieves the subject of insomnia, dyspepsia, and irritability of manner and temper. It restores the failing vigor and energy of character. This celibism (a coined word: the morbid state of celibacy) is exceedingly common and worthy of the practitioner's fullest attention as being the cause of many abnormal states not correctly understood, and not rationally and efficiently treated. The use of the term neurasthenia has done much to make the subject still more cloudy and obscure.

Nickel acts as a sedative and tonic of peculiar and elective power in controlling the damaging effect of sexual vice on the nervous system in masturbation and onanism. The cases just described are met with in the continent and morally pure, suffering from the misinterpreted impressions of a life at variance with nature, but in masturbation is found the grave injury of an active vice harmful in proportion to the frequency with which it is practised, up to the degree of absolute exhaustion of organic function. The symptoms of masturbation are many, striking, and grave. The diseased state arising from it is frequently overlooked, misdiagnosed, and mistreated. It can be recognized with great certainty by its physical and nervous symptoms, which present a clear and distinct picture of perverted sexuality. The masturbator[17] with increased hunger shows no proportionate gain in weight, but soon, with deranged and weakened digestion, there appear wasting of the body, lassitude, meteorism, cramps, and vomiting after meals. The voice is weakened; the words imperfectly articulated. There is much susceptibility to cold. The nervous system is deranged and disturbed. There are vertigo and insomnia, nerve pains and increased cutaneous sensibility, convulsions and epilepsy, impaired vision and aural tinnitus, motor and sensory paralysis. The intellect and memory are enfeebled. The mind is drowsy, and even light work is too great a task. Moroseness, melancholy, and disgust of life prevail. Mania may appear, or suicide end a miserable existence. Inspection of the external genitals can often prove the masturbator. The testicles are atrophic, as is also the shaft of the penis, which, when flaccid, is elongated, while the glans penis is pale and, by comparison, too prominent. In the female there is great hyperesthesia of the clitoris and its sheath. The labia are red, dry, and irritated. The main factor for a correct diagnosis which is constant and

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17 H. Fournier, "De l'Onanisme," 5th ed., 1893.

accurate is the behavior of the heart.[18] It is slightly dilated or hypertrophied, is irritable, and the contractions are invariably too rapid, from 120 to 140 pulsations per minute. Excluding so-called idiopathic tachycardia, nicotine poisoning, exophthalmic goiter, and pulmonary tuberculosis, the heart of the masturbator is clinically a correct index of the nature of the trouble. In this expanded and rapidly throbbing organ the first sound at the apex is not clear, and the second sound at the base or over the aorta is accentuated. The pulse is soft and rapid.

In the treatment of masturbation, the subject must have the consequences of his pernicious habit clearly explained: the great and direct injury to his health, a future of idleness, solitude, and contempt. No effort should be made to force a confession or declaration of his fault. He must be convinced that it is vulgar and without advantage, destructive to any remains of pride or spirit. He must compel himself to daily study or labor, without which all treatment fails, an idle life being in no other instance more harmful to health or its recovery. For the faulty nutrition and emaciation a milk diet is so essential that failure to help the case results from its non-employment. The sulphate of nickel has the effect of reanimating and invigorating the victim, restores sleep, diminishes the rapid action of the heart, and seems to make the subject realize the very injurious effects of his secret vice. When the case is complicated with the obsession of lost manhood from correspondence with advertising specialists and from reading the secret horrors of their literature, the case assumes a hopeful feature, and recovery is all the more certain where good fees have been offered up in vain in attempting to recover the lost or imperiled power.

There is a third class of morbid excitation of the generative organs distinct from celibism and masturbation: the too frequent venereal dreams and seminal emissions during sleep, mostly found among young men either in vigorous health or physically debilitated. The nervous system does not show the abnormalities of the other classes, and only a few of such patients become seized with a fear of impotency, extra or pre marital. Instances, however, can be found where marriage has been shunned by such unfortunates who, entirely forgetful of consulting a physician, have condemned themselves to single life in abject despair. The nickel salt here, as in the former conditions, gives relief. It reduces the spontaneous pollutions to one or two monthly, and acts better than do bromides, camphor, sodium borate, or other remedies heretofore commended.

These observations do not limit or conclude the useful medicinal applications of nickel. The interesting and beneficial virtues described are only a part of those belonging to this metal. It is probable that among infectious diseases of acute or chronic form one or more may be found that will yield to its antiseptic or antiparasitic powers, so that its systemic administration may overcome some affection which, so far, has baffled the physician's efforts to conquer.

[18] G. Bachus: "Ueber Herzerkrankungen bei Masturbanten," Deutsch. Arch. für klin. Med., lix, 1894-5; also his inaugural thesis.

CHRONIC ACETANILIDE POISONING A PERFECTLY DEFINITE SYMPTOM-COMPLEX.

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It is not generally recognized by the profession that the ingestion of the aniline derivatives of the antipyretic group is capable of producing profound pathological changes in the blood vascular system, with the production of a perfectly definite symptom-complex, nor is it a well-recognized fact that one of these products, acetanilide, because of its cheapness and extreme toxicity, and of the fact that it is the chief constituent of many of the so-called headache or neuralgic powders or tablets commonly dispensed over the counter both by pharmacists and the ordinary country storekeepers to the laity, is not only responsible for most cases of poisoning by this group, but also for the production of a drug habit or addiction in every way comparable to that of opium or alcohol. If we stop, however, to consider the large number of secret nostrums on the market containing as their chief ingredient acetanilide which are dispensed without prescription for the cure of headache, neuralgia, neurasthenia, and the like, the marvel is that chronic poisoning or acetanilide addiction is not an exceedingly common complaint, rather than the rare condition that a study of the literature would lead us to suppose. The symptoms excited by the continued ingestion of acetanilide are so characteristic and highly suggestive of poisoning by this drug that it seems rather unusual to note that many of the cases of chronic acetanilide poisoning or addiction recorded in the literature have been entirely overlooked by competent observers, the condition being diagnosed as cardiac disease, tuberculosis, polycythemia, neurasthenia, mediastinal growths, and the like. This error in diagnosis, I believe, is made possible, as in most instances of drug addiction, by the patient's deception.

A study of the cases recorded in the literature and those hereinafter to be reported proves that the ingestion over a considerable period of time of acetanilide or related coal-tar products is productive of a definite symptom-complex which is highly suggestive, if not absolutely diagnostic, of poisoning by this group.

The subjective symptoms are great general weakness, nervous excitability, insomnia, loss of appetite, digestive disturbances, palpitation, dyspnea, numbness and weakness of the extremities, pain in the region of the liver and spleen, and faint attacks.

The chief objective symptom is cyanosis, which is often extreme, but usually fluctuating in intensity, accompanied by marked pallor of the mucous surfaces and without clubbing of the fingers.

The blood-changes are quite characteristic, and due to the destructive action of a hemolytic poison circulating in the blood-stream, which produces

a secondary anemia variable in degree. The erythrocytes are diminished in number; they often present nucleated forms, show granular stippling, stain poorly, and are variable in size and form. There is usually a moderate leucocytosis of the polymorphonuclear variety, and there is often a relative increase of the lymphocytes. The appearance of the blood as it stands upon the finger-tip or the ear is very suggestive; it is either of a bluish-black color or chocolate in appearance. The coloration of the plasma renders the estimation of the hemoglobin quite difficult. Most observers state that the hemoglobin is diminished, which I believe is true; but I must confess with Stewart that it is almost impossible in these cases, owing to the coloration of the plasma, to measure the hemoglobin accurately.

The spleen has been found enlarged in most of the well-observed cases, and it is usually tender both on palpation and percussion. The liver is slightly increased in size and is also tender on pressure.

The heart is usually found enlarged, the transverse diameter being increased and the apex beat displaced downward and outward. The heart sounds are feeble, and adventitious murmurs are frequent. Systolic mitral and tricuspid murmurs are common, as are basic systolic murmurs. These murmurs are probably dynamic in origin and due to the loss of tonicity of the heart muscle, as they disappear *pari passu* with the diminution in size of the heart and improvement of the blood on the withdrawal of the acetanilide. The mitral and tricuspid murmurs are doubtless caused by relative leakage, while the basic murmurs are hemic in origin.

The urine is usually dark brown or black in color, and gives the characteristic indophenol reaction. It may contain blood-pigments in the form of methemoglobin or hematoporphyrin. Bilirubin is common, and glycuronates may be present. It is interesting to note that the ratio of the sulphates has been found reversed. In my first case the ratio was 16 to 1, only a comparatively few milligrams of the oxidized sulphur being eliminated in the form of inorganic sulphates. Dextrose was found in both of my cases, and probably exists in small amounts in most cases.

I have been unable to find any mention in the literature of trophic changes in the way of ulcerations of the skin, such as occurred in my first case. That these ulcerations were due to the effects of acetanilide seems probable, as most other causes could be excluded.

The diagnosis of chronic acetanilide poisoning should be attended with no great difficulty provided we are mindful of the fact that when this drug is circulating in the blood-stream it acts as a most virulent hemolytic poison and creates the complex of symptoms above narrated. It is quite obvious, however, that in our differentiation we must exclude those diseases which are accompanied by more or less persistent cyanosis, namely, congenital heart defects, grave cardiac insufficiencies, certain pulmonary diseases, arteriovenous aneurism, and chronic cyanosis with polycythemia. All of these conditions may in turn be differentiated by a most careful and painstaking examination; but in order to determine the presence of the last-named disease, we must in addition make repeated blood counts and hemoglobin estimations. It is, indeed, very probable

that some of the reported cases of chronic cyanosis with polycythemia have actually been cases of chronic acetanilide poisoning, having, as in the case of Cabot's and in my first case, a temporary, but very decided polycythemia. It is a fact that the symptoms created by the ingestion of acetanilide mimic very closely those common to polycythemia. The differentiation, however, between these two conditions may easily be made if we remember that acetanilide and allied products are excreted with the urine, and may be detected by appropriate and simple tests.

In conclusion, I would state that it is extremely interesting to notice the rapid improvement of the patient which follows upon the removal of the drug. Within a few days the cyanosis gives way to a distinct pallor of the skin and mucous surfaces. The urine no longer is dark brown, the indophenol reaction is absent, and blood-pigments cease to be found. The blood is rapidly regenerated; it loses its dark-purple color, and the hemoglobin content and red-cell count rise rapidly to normal. Associated with this improvement in the blood is a diminution in the size of the liver and spleen, together with a marked diminution in the size of the cardiac area, improvement of the tone of the heart sounds, and a diminution or loss of the cardiac murmurs. With these changes the appetite soon returns, the mentality clears, the nervous excitability disappears, the nutrition improves, and the gain in flesh and strength soon restores the patient to the normal.

The first case to which I wish to direct your attention is one of chronic poisoning the result of the acetanilide habit extending over a period of four years, and due to the ingestion of a compound acetanilide tablet containing 5 grains of acetanilide. The patient was in the habit of taking 10 to 15 of these tablets daily, thus receiving a daily dose of from 50 to 75 grains of the pure drug. She took these tablets secretly for about four years, obtaining them from a nearby druggist. It was not until her second visit to the hospital, however, that the habit was discovered, and then only by accidentally finding the tablets among her belongings. She very reluctantly confessed, and it was with much difficulty that we were able to learn the exact daily dose which she had been in the habit of taking.

Immediately upon the withdrawal of the drug, her cyanosis disappeared and the circulatory symptoms began to improve, and within a fortnight the bluish-black discoloration of the blood could not be seen. The urine assumed its normal color; the liver and spleen ceased to be tender and gradually diminished in size to the normal. She developed, however, great nervous excitation, suffered from insomnia, lost her appetite, presented a fine tremor of the extremities, and stated that she had a fearful craving for the drug, felt sure she could not live without it, and knew that she would relapse again upon leaving the hospital. She remained in this nervous state for a period of about three weeks, when the craving for the drug gradually disappeared, and on her dismissal from the hospital the desire for it had ceased.

The patient first consulted me Sept. 5, 1906, when I made the following notes: Very cyanotic, no edema, spleen palpable and tender, apex beat in fifth interspace ½ cm. to the left of the left mammillary line, systolic apex murmur

conducted to the left axilla, moderate emphysema, no râles; pulse rapid, easily compressible; vessels not thickened, systolic tension 130 mm. Hg.

The red-cell count was 9,200,000. On Sept. 9th, the red cells had diminished to count 7,500,000. The stained specimen showed no apparent leucocytosis, no nucleated red cells, considerable deformity of them, but no polychromatophilia. The blood was of a dark-purple color, and it coagulated rather slowly. The urine was very dark brown; it contained no albumin, sugar, or free blood-cells. The patient denied absolutely having taken any drug for pain.

The cardiac condition being insufficient to account for the intense cyanosis, I was led, in consideration of the enlarged and palpable spleen, the chronic cyanosis, the high red-cell count, the peculiar coloration of the blood and urine, and the apparent high hemoglobin value, together with an absolute denial of the taking of any drug whatever for pain or otherwise, to the probable diagnosis of chronic cyanosis with polycythemia, due to some hemolytic agent circulating in the blood-stream, possibly intestinal in origin, and perhaps similar to that in the case recently reported by West.

My attention was again directed to the case July 14, 1908, when she entered my service at the Samaritan Hospital and presented the following history:—

Miss Elizabeth G., aged 30 years; a postal clerk by occupation. Complained of great weakness, palpitation, faint attacks, dyspnea on exertion, and a peculiar fluctuating bluish coloration of the skin, lips, and fingers. Her family history is without import.

Personal History.—She has had all the diseases of childhood. Had a right-sided pleurisy three years ago. The menstruation was established at 15 years of age; it has been irregular, very scanty, and with much pain. For the past two years it has been of an unusually dark color, and of the consistency and appearance of thin tar. She was operated on six years ago for a movable right kidney. For two years she has had recurring faint attacks, with marked dizziness, tinnitus, nausea, and vomiting. During these attacks her vision gradually becomes dimmer, until she is almost blind. She has never lost consciousness. She has noticed at the time of the occurrence of the attacks that the bluish discoloration of the skin is most intense. She denies emphatically having taken tablets or powders for the relief of pain or headache. Recently she has had severe neuralgic pains in the region of the spleen.

Examination.—She is slightly built, somewhat emaciated, and very cyanotic. The coloration resembles most closely that seen in cases of morbus cæruleus. There is a distinct fullness of the face, but no apparent edema; the lips, ears, fingers, and toes are almost purple. Her conjunctivæ are pale and cyanotic, and the skin of the whole body is a bluish black. There is no edema of the extremities, and no clubbing of the fingers or toes. The buccal and pharyngeal mucous membrane is very pale; the tongue is blue and is coated with a whitish fur.

Lungs.—Apart from the evidence of a slight degree of pulmonary emphysema, nothing abnormal was detected.

Heart.—The apex beat is palpable in the fifth intercostal space 9 cm. to the left of the midsternal line; no friction or thrill can be detected over the precordium. A distinct systolic epigastric pulsation is present. There is no tugging or Broadbent sign.

The vertical cardiac dullness begins at the fourth rib, and the transverse dullness begins at the right edge of the sternum and extends 12 cm. to the left. A soft, blowing, systolic murmur, having its point of maximum intensity at the apex and conducted to the axilla, is heard. The murmur does not totally replace the first sound. A softer systolic murmur is also heard, localized to the tricuspid area. The pulmonic second sound is accentuated. A systolic murmur is heard in the carotids and subclavians and over the abdominal aorta. No basic murmur is detectable. The pulse is soft, regular, rapid, and easily compressed. The vessels show no evidence of thickening; the systolic blood-pressure is 120 mm. Hg. There is no visible pulsation of the jugular veins.

Spleen.—The dullness of the spleen in the midaxillary line is at the level of the fifth rib; it extends downward and inward to the costal border. The organ is easily palpable and is of firm consistency; its border is not irregular, but it is quite tender both on palpation and percussion.

The *abdomen* is symmetrical, and it is generally tympanitic. There are no enlarged veins. In the right loin there is a scar, the result of a transverse incision 14 cm. in length, the coloration of which is of a dark purple.

Bones.—Percussion of the ribs, sternum, and long bones of the extremities brings out considerable tenderness. There are no enlarged lymph-nodes.

Nervous System.—The cranial nerves: The pupils are midwide, equal, responsive to light and accommodation. They act consensually, and respond actively on each side to irritation of the cervical sympathetic. The visual fields are not contracted. Rotation of the eyeballs is normal. The media are clear, and the optic discs, although pale, appear normal. The face and tongue muscles functionate normally.

The motor power is normal. Although the patient complains of numbness in the hands and feet, there are absolutely no objective sensory disturbances, no ataxia; the sense of position is normal, and there is perfect preservation of the stereognostic sense. There is no Rombergism.

Reflexes.—The deep reflexes are lively; no true clonus or Babinski sign exists on either side. The superficial reflexes are normal. The mind is perfectly clear.

Blood.—The blood as it stands on the ear or finger is of a bluish-black color. The red cells stain well. There are no nucleated red cells; slight deformity exists, but there is no definite poikilocytosis. No remarkable differences in size of the red cells is present. The blood-count showed 2,142,610 reds and 7000 whites. Differential count of 500 whites showed: Lymphocytes, 36 per cent.; polymorphonuclears, 60 per cent.; eosinophiles, 3 per cent.; transitionals, 1 per cent.

It was impossible accurately to measure the hemoglobin because of the coloration of the blood; it appeared, however, to be 100 per cent. plus.

The *urine* is of a dark-red color, which darkness increases on standing. The specific gravity is 1030; the reaction is neutral; it contains no sugar, albumin, or blood-cells; with the benzidine test no reaction for occult blood occurred, and with the Zeiss hand spectroscope no absorption bands were detected. Prof. Holmes C. Jackson kindly examined the urine for hemoglobin or its derivatives, and found none.

Although the patient remained in the hospital for three months, there was no material improvement in her general condition. The cyanosis; the enlarged, painful spleen; the cardiac dilatation, and associated murmurs were unaltered.

A blood-count taken just before her departure showed the following: Red cells, 2,700,000; white cells, 7800. Polymorphonuclears, 62 per cent.; large lymphocytes, 16 per cent.; small lymphocytes, 20 per cent.; eosinophiles, 1 per cent.; transitionals, 1 per cent.

There were no nucleated red cells, no great deformity of them, and they were

Case of chronic acetanilide poisoning showing marked cyanosis and characteristic facial expression.

Case of chronic acetanilide poisoning showing trophic ulcer on left leg.

nearly uniform as to size. The average systolic blood-pressure, deduced from a large number of observations, was 110 mm. Hg.

The sphygmogram which I pass about shows quite well this low tension. The urine remained of the same dark color, and showed no occult blood or spectroscopic evidence of hemoglobin or its derivatives.

The patient re-entered the Samaritan Hospital October 5, 1909. She is in every way worse, there is much general emaciation, the cyanosis is intense, and her appetite is poor; she states that she had slept badly; she seems very morose and apathetic, and she is in an extremely melancholy frame of mind.

Sphygmogram. Miss G. Polycythemia. Arterial tension 130 mm. Hg. Tracing from left radial. Radials showed no change when arms were elevated above head.

October 26, 1909, the following notes were dictated: The patient's skin and mucous surfaces are deeply cyanosed; the face is distinctly swollen; there is no edema of the extremities, but they are very cold. Over the anterior surface of the left tibia is a sharply circumscribed area of necrosed tissue, the result of a previous bruise; it shows no tendency to heal, and presents unhealthy granulations; its coloration is dark blue. A small depressed scar, the result of an ulceration, is present on the lower part of the left pinna, and a larger one of the same character is found in the scar resulting from her previous operation for anchoring the right kidney.

Heart.—A distinct epigastric pulsation is present. The apex beat is in the fifth interspace, 1 cm. to the left of the left mammillary line. A systolic murmur is heard at the apex, and transmitted to the left; it is quite as well heard at the junction of the fourth rib with the sternum. A very soft systolic murmur localized to the tricuspid area is heard. A systolic pulmonic murmur is also present. A venous hum is detectable, especially in the vessels of the left side of the neck. The pulse is soft, regular, easily compressed, and 90 per minute.

The *liver* dullness begins at the fifth rib, and extends downward 1½ cm. below the costal border. The liver is palpable and slightly tender; its lower margin is smooth.

The *spleen* dullness begins in the midaxillary line at the sixth rib, and extends downward and inward 1 cm. below the costal arch. The spleen is easily palpable and very tender.

The *abdomen* is somewhat tender, but otherwise normal. The uterus and adnexa appear normal. The menstruation is scant, very dark, and of a tarry consistency.

The cranial nerves functionate normally. The retinal and optic discs are devoid of any pathological change. Motion and sensation are normal.

A blood examination made by Dr. Carey, pathologist to the hospital, showed the following: Red-cell count, 3,840,000; white-cell count, 9720; smears showed moderate variations in the size of the red cells, but very little deformity; no nucleated red cells, no stippling.

Differential count: Small mononuclears, 21.5 per cent.; large mononuclears, 5.5 per cent.; transitionals, 3 per cent.; polynuclears, 68.5 per cent.; eosinophiles, 0.5 per cent.; mast cells, 1 per cent.

The urine is dark red, slightly acid in reaction; it contains no albumin, sugar, casts, or blood; its specific gravity is 1025.

A Von Pirquet test was negative.

Despite her denial of taking drugs other than those given to her by her physician, which upon inquiry proved to be tonics, I firmly believed that her symptoms were induced by some hemolytic agent, probably a coal-tar derivative, and advised watching her closely. We were rewarded two weeks later by finding on her person the tablets which I have previously mentioned. An immediate examination of the urine for acetanilide gave, by the test of Müller, a well-marked indophenol reaction, which was positive for four days after the withdrawal of the drug. A specimen of urine was sent to Victor C. Myers, Professor of Physiological Chemistry at the Albany Medical College, to whom I am indebted for the following exhaustive report:—

URINE EXAMINATION.

A twenty-four-hour specimen was obtained on November 3, 1909, and after preliminary examination was preserved with toluene. Volume, 670 c.c. Color, a deep brown or brownish red (on further standing the urine became black). Odor, rather strong and somewhat peculiar. Sp. gr., 1026. Reaction, slightly acid. Sediment, urine slightly turbid, but no perceptible sediment. Microscopical examination, entirely negative.

Sugar.—The urine gave a strong reduction with both Benedict's and Fehling's solutions, and a slight reduction was obtained with Benedict's solution on adding only 1 drop of urine. When the phenylhydrazine reaction was applied to diluted urine, a bulky precipitate of phenyldextrosazone crystals settled out. These were easily identified microscopically. The urine showed almost no rotation.

Protein.—Heller's test with nitric acid was negative.

Indican.—A slight reaction was obtained with Obermayer's reagent and chloroform.

Acetanilide.—The urine was found to give a very strong indophenol reaction, but the alphanaphthol reaction for acetphenetidin was entirely negative. The indophenol reaction was, without doubt, referable to acetanilide. An attempt to isolate a crystalline body with ether and benzene was unsuccessful. To this end 300 c.c. of the urine were filtered, boiled with strong sulphuric acid, cooled, extracted several times with ether, the ether distilled off, the residue neutralized, and again extracted with ether. After distilling off the ether the second time, the residue was extracted with benzene and allowed to evaporate spontaneously, with negative result. The residue after the benzene extraction was still found, however, to contain a body capable of giving a strong indophenol reaction, though it seemed impossible to isolate this substance in crystalline form.

Sulphates.—The ethereal sulphates were very high, probably due to combination with some acetanilide derivative, such as acetylparaminophenol. The sulphate elimination in grams of H_2SO_4 per twenty-four hours was 0.046 Gm. for the inorganic sulphates and 0.719 Gm. for the ethereal sulphates, an inversion of the normal ratio. This amount of ethereal sulphate would be sufficient to combine with about 1.1 Gm. of acetylparaminophenol.

Glycuronic Acid.—It seemed of interest to learn whether or not acetanilide derivatives were eliminated in combination with glycuronic acid as a glycuronate. The reduction with Benedict's and Fehling's solutions might, in part, have been due to glycuronic acid, though dextrose was found to be present. The fact that there was almost no rotation in the presence of a considerable quantity of dextrose would point to the presence of some levorotatory substance such as a glycuronate. Tollen's phloroglucinol reaction was moderately strong, but a reaction with orcinol could not be obtained after boiling the urine with acid. It seems possible that glycuronic acid was present at least in small amount, though the evidence on this point was not conclusive.

Blood and Blood-pigments.—The guaiacum and benzidine blood-tests were entirely negative with carefully controlled solutions and reagents. No spectroscopic absorption bands could be obtained with the urine or slightly acidified urine. Heller's test was tried several times with uniformly negative results (boiling with caustic alkali). The phosphate precipitate was collected on one occasion and extracted with acid alcohol. The alcohol assumed a dark color, but no absorption bands were noted. In the presence of blood, the absorption spectrum of hemochromogen should have been noted. A mixture of equal parts of a saturated barium hydroxide solution and 10 per cent. barium chloride was found to precipitate the pigment. The precipitate was then extracted with acid alcohol. The solution showed absorption spectra of none of the blood-pigments. Neither methemoglobin nor hematoporphyrin or other blood-pigments could have been present.

Dark Urinary Pigment.—The dark color of the urine was in all probability referable to urobilin (pathological urobilin of Jaffé). Twenty-five c.c. of urine were precipitated with 20 c.c. of equal parts of baryta water and barium chloride. After extracting the pigment with acid alcohol, the solution was observed spectroscopically. No absorption bands for hematoporphyrin were noted, and only very faint bands for urobilin. Chemical tests for urobilin, such as Jaffé's zinc chloride reaction in ammoniacal solution, were questionable. The pigment was found to be precipitated by both lead acetate and lead subacetate. It was also found to be salted out by ammonium sulphate to saturation in acid solution. This is the basis of G. Hoppe-Seyler's method for the estimation of urobilin. Accordingly, 50 c.c. of urine were precipitated, washed with saturated ammonium sulphate, and extracted with equal parts of absolute alcohol and chloroform. This readily extracted the pigment. Upon purification an amount of urobilin equivalent to 0.2 Gm. for the twenty-four hours was obtained.

Summary.—In a specimen of urine obtained on November 3, 1909, the volume was 670 c.c., with a sp. gr. of 1026. The color was of a deep brown or brownish red when passed, but on long standing turned an ink-black. Acetanilide was easily demonstrated by the indophenol reaction, and acetphenetidin was shown to be absent. The urine gave a strong reduction with both Benedict's and Fehling's solutions, and upon applying the phenylhydrazine reaction an abundant precipitate of dextrosazone crystals was obtained. These were easily identified microscopically. It seemed probable that glycuronates were present, though the evidence on this point was not conclusive. The sulphate ratio was found to be reversed, being 16 to 1, only a comparatively few milligrams of the oxidized sulphur being eliminated in the form of inorganic sulphates. Blood-pigments were shown to be absent both chemically and spectroscopically. Special care was taken to detect both methemoglobin and hematoporphyrin, but they were absent. Chemically the pigment of the urine was identified as the pathological urobilin of Jaffé, which is occasionally found accompanying a destruction of the blood-corpuscles. A quantitative estimation of this urobilin was made by the method devised by G. Hoppe-Seyler and found to be 0.2 Gm.

CASE II.—Mrs. A., married, aged 52 years, consulted me August 20, 1910, complaining of great exhaustion, considerable loss of flesh, shortness of breath on exertion, loss of appetite, and palpitation.

Family history unimportant.

History of Previous Condition.—Patient stated that her menstruation had always been regular until five years ago, when it ceased. At that time she developed very severe headaches, directly over the vertex, for the relief of which she obtained some "antipain" pills, using from 50 to 75 of these pills each week; this practice she has continued ever since.

At the present time she is weak and complains of pain in the region of the spleen, dyspnea, and palpitation of the heart.

General Condition.—She is slightly built; the muscles are flabby; there is some general emaciation; there is no edema, but there is marked cyanosis of the lips, ears, tongue, buccal and pharyngeal mucous membranes, fingers, and toes, and there is also considerable pallor. Her physician states that the cyanosis is variable; some days she is as blue as a huckleberry; at other times she is simply pale, with slight cyanosis of the lips and fingers. She is very restless at night, sleeps poorly, and is in an extremely nervous and irritable condition.

Physical Examination.—Pupils are contracted; they react to light, accommodation, and consensually; the ocular movements are normal; the lids move normally; the hearing is acute in both ears; the facial muscles functionate normally; the senses of taste and smell are normal; motion and sensation are preserved.

The Reflexes.—The tendon reflexes are lively; the superficial reflexes are present, but not very active.

The Heart and Arteries.—The peripheral vessels do not appear thickened; the pulse is regular and easily compressible; the rate is 100 per minute; the systolic pressure is 115 mm. Hg. The apex beat is in the fifth interspace at the junction of the left mammillary line, at which point a soft systolic murmur is heard, transmitted to the left to the midaxillary line. The pulmonic second sound is accentuated. The aortic second sound is normal; there is no venous hum or visible jugular pulsation. The blood is bluish black in color. It was impossible to measure the hemoglobin accurately with the Sahli instrument, but it seemed to be 100 per cent. Microscopic examination of the blood showed a slight deformity of the red cells, no polychromatophilia, no nucleated red cells, and no granular stippling. There was no apparent leucocytosis. Unfortunately no blood-cell count was made.

The abdomen is tender and universally tympanitic; there are no enlarged glands or herniæ; in the left hypochondriac region and extending downward and inward almost to the umbilicus is a tumor mass having a distinct notch and an even, roundish border, which moves on inspiration and corresponds to a dullness beginning in the midaxillary line at the seventh interspace and extending downward and inward. This is doubtless the spleen, and it is tender on palpation and percussion. The kidneys are not palpable. There is no abdominal ptosis. The liver dullness in the right mammillary line begins at the fifth rib and extends 1 cm. below the costal border. The lower margin of the liver feels normal, but the organ is decidedly tender.

The lungs show nothing abnormal. The urine is of a dark color; its specific gravity is 1010. It contains no albumin and does not reduce Fehling's solution; there is no occult blood present.

Urine Examination.—It was possible to obtain only a small specimen of urine in this case. The indophenol reaction was found to be strongly positive. Inasmuch as the alphanaphthol reaction for acetphenetidin was negative, the indophenol reaction was very evidently due to acetanilide. The urine was found to give a moderate reduction with Benedict's solution. Upon applying the phenylhydrazine reaction, dextrosazone crystals were obtained, which were easily identified microscopically. The rotation of the urine was found to be slightly levorotatory,—0.2 in a 10 cm. tube.

Subsequent History.—The patient was easily induced to give up the habit of taking the tablets (which proved to be acetanilide), and within three months she was restored to perfect health,—the spleen diminishing rapidly, the heart dullness decreasing to the normal, and the cyanosis being displaced by a normal pink coloration of the mucous membranes.

From this study the following conclusions may be drawn:—

First.—That the continuous ingestion of acetanilide or allied products

creates a perfectly definite symptom-complex, characterized by cyanosis, enlargement of the heart, spleen, and liver, a definite blood-picture, and characteristic urinary findings.

Second.—That the acetanilide habit or addiction is a well-established one and its enslavement is comparable to that of opium or alcohol.

Third.—That acetanilide is a most virulent hemolytic poison which produces definite changes in the blood vascular system.

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DISCUSSION.

Dr. Brown: I am especially interested in acetanilide poisoning. You may remember a remarkable case which I reported in the American Journal of the Medical Sciences, fifteen years ago, of an individual taking 60 grains of acetanilide within two hours. The patient died within six days, having had the symptoms which have been described so well in this paper, together with extreme nausea and the passing of claret-colored urine and reddish-black stools. Since that time attention has been called to the commonness of acetanilide poisoning, and I think the most important part of this paper, and of Dr. Wiley's work in Washington, has been to make known the dangers of the coal-tar products, and to bring before us the fact that we cannot afford to overlook them in cases of migraine and nervous headache. Persons acquire the habit with great ease. I have repeatedly come across this habit in people who will tell you nothing about their nervous symptoms and are very loath to tell you they are addicted to the use of such drugs. There is a craving for the temporary relief which some patients get from headache remedies containing acetanilide, of which they are ashamed, and which they regard as a habit which they know will be dealt with immediately if it comes to light. I have known a patient who got rid of a dollar bottle of such a remedy in a few days. She was addicted to the use of opium, which was first given to her by a physician, and then alcohol. Finally realizing that she was addicted to these habits, her physician succeeded in breaking them, but in doing so substituted the habit of taking one of these. It says on the bottle that there are 3 grains of acetanilide in each teaspoonful, and a patient usually takes a heaping teaspoonful, which amounts to 3 level

ones at least, or about 10 grams a dose. If patients say they take 2, you may be pretty sure they take 5 or 6; so that the daily doses of acetanilide taken by these people are enormous. My fatal case took within a few minutes 60 grains and never recovered consciousness; he died within six days. The case showed that there was destruction of red corpuscles to about ⅛ the normal. A large number of the red cells, however, were increased in diameter, and there were numerous nucleated red cells, many of them undergoing mitosis. In conjunction with the destruction of red corpuscles, there was an increase in size of some of the reds in proportion to the resistance. In this particular the resemblance to pernicious anemia is interesting. The nature of the pigment in the urine interested me greatly at the time. I recall one case, a man suffering from migraine, whose cyanosis was sufficient to lead me to believe that he was in danger. He would take 3 or 4 of the compound acetanilide tablets at one time. Why he did not kill himself, in view of the death-dealing dose of 60 grains of unadulterated acetanilide, I do not know. I presume that in time we get a certain resistance to these things. We must realize that this is one thing which people are loath to confess, and that they must be watched as morphine cases are watched. Stengel and White, of Philadelphia, reported the case of a physician's daughter who was in a Philadelphia hospital two or three weeks before they found a bottle of the tablets under her pillow, but not until she had been caught would she confess.

Dr. Stewart: Several points in Dr. Gordinier's paper might well serve as illustrations for my own paper at this meeting.

I had a classmate at the Philadelphia College of Pharmacy who was thrown out on examination. He, therefore, concluded that he would find an easier way of getting a living than by practising legitimate pharmacy; so he organized what he called a "chemical company" for the manufacture of acetanilide headache powders. A fanciful name was devised by his lawyer for this compound, and he placed it on the market. His next move was to create a demand by advertising the product in the medical journals. In this he was eminently successful. His sales were enormous. I remember seeing a large stock of this compound in the drug department of one of the principal San Francisco hospitals, where I was told that all the leading physicians in California were using it. The journal of the American Medical Association accepted the advertisements, and the profession generally employed it in their practice. Through physicians' prescriptions it was introduced to the lay public and then became a popular nostrum. My classmate's share of the profits was more than two million dollars. I am also acquainted with the history of another acetanilide compound headache remedy, introduced by a well-known manufacturing house, the sale of which has amounted to fifty thousand dollars a year. This product was introduced directly to the laity by advertising in street cars, elevated railroad cars, etc. You will probably remember the case of the young Vassar girl, the daughter of a doctor who prescribed for her one of the acetanilide compounds without warning her against its abuse. She became addicted to the acetanilide habit, lost her reason, and finally walked into the lake and drowned herself. Much of what is evil in the nostrum business has been due to the abuse of the trade-mark system referred to in my paper. A fanciful name is given to an acetanilide compound, which conceals its identity, and it is introduced by advertising as a specific for headache. This evil has been in part corrected by the Pure Food and Drugs Act, which requires the amount of acetanilide present to be printed on the label. If physicians would confine their prescribing to legitimate pharmaceuticals, as prepared by decent manufacturing houses and supplied by pharmacists in the form of regular prescriptions, this exploitation of the public would be avoided.

Dr. Gordinier: I would like to ask Dr. Brown if he had an autopsy of his case. I can find no well-reported autopsy of cases of this kind, and it seems to me that a well-reported autopsy would throw a great deal of light on the subject.

Dr. Brown: There was an autopsy in that case, but it was not such a one as would probably satisfy your desire for knowledge. I did not know at the time, although we suspected the presence of a coal-tar product, exactly what was wrong with the patient. I think the records may, however, show something of what you want to know. I have not read the findings for many years. I want to mention a case of poisoning that was referred to me by a surgeon presenting extensive ulcers of the leg, upon which acetanilide had been used as a dusting powder —a danger not to be overlooked.

CONCERNING THE THERAPEUTIC VALUE OF SODIUM CACODYLATE.

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ALBANY, N. Y.

At the eighth annual meeting of this Society, May, 1907, a paper was presented embodying the results of certain investigations by Holmes C. Jackson and myself, entitled "The Physiologic Action, Elimination and Therapeutic Application of Sodium Cacodylate, Used Hypodermatically."[1]

Inasmuch as certain authorities have so emphatically insisted that sodium cacodylate is possessed of no arsenical properties, either physiologic or therapeutic,[2] it may not be amiss for me to summarize our findings as to that particular point, and, at the same time, to state that other observers, notably Runnels,[3] have confirmed many of our statements. Our experiments were conducted with great care at Bender Hygienic Laboratory, and were made not only upon dogs and rabbits, but upon human beings. We found that the body "possesses the power of decomposing the organic compound into an active inorganic form" when injected intramuscularly; that it is "eliminated in the form of arsenates by the urine and feces; the urine of patients under its influence yields arsenates and reacts to Marsh's test;" that it has a distinct toxic effect, and may be recovered in the form of inorganic arsenic in various tissues of the body, such as the liver, muscle, and bone-marrow.

The therapy of the hypodermic use of sodium cacodylate is based upon the observation of several thousand cases treated by the writer or reported to him by 76 other observers, many of the latter trained clinicians of wide experience. The only untoward symptom observed or reported was a transitory discomfort at the site of injection when the larger doses (0.3 to 0.6 Gm.) were used.

It is generally accepted that the value of arsenic as a therapeutic agent, where indicated, is limited only by its toxicity, evidenced mainly in the gastro-intestinal tract; and, in the opinion of the writer, herein lies the justification for the use of sodium cacodylate hypodermically, for our experiments have shown that much of this drug is changed into inorganic arsenic, is stored in the tissues and utilized as rapidly as it can be taken care of and without effect on the mucosa of the digestive tract. Experience has taught us that in giving small doses and in giving our injections for several days, with intervals of non-treatment for fear of toxic results, we erred on the side of prudence,

[1] Journal of the American Medical Association, June 22, 1907, p. 2090.

[2] "The Inefficiency of the Di-Sodic-Methyl-Arsenate as a Therapeutic Agent," T. R. Fraser, The Lancet, 1903, vol. cliv, p. 304.

[3] S. C. Runnels: New York Medical Journal, Dec. 3, 1910.

and that in most cases satisfactory results were obtained only by using relatively large doses daily without intermission, and often for several weeks, this being especially so in anemias of long standing.

There have been reported to me 14 cases of pernicious anemia treated with sodium cacodylate. Of these, 4 had short periods of improvement, alternating with exacerbation of the symptoms, and finally died. Of the remaining 10, reported as cured, 5 have been but so recently discharged (three, five, six, eight, and nine months) that we cannot claim them as cures, even though they are reported by careful observers, and have every evidence of recovery. The other 5, however, seem to be properly classed as well, for their discharges from treatment with no recurrence of the symptoms are, in point of time, respectively, fifteen months, eighteen months, twenty-two months, twenty-five months, and thirty-seven months. In these 5 cases careful blood-counts were made at frequent intervals, and from the character of those reporting, as well as from the blood-pictures and the case histories, I have no doubt as to the correctness of the diagnosis.

The history of 1 case, the one longest recovered, is very complete; and as the dosage used was much smaller than was used in the other cases, I give it here:—

Patient first seen September 6, 1906.

Diagnosis.—Pernicious anemia, achylia gastrica.

Complaints.—Indigestion and loss of strength.

Family History.—Not important. No history of cancer or tuberculosis.

Past History.—Has been an exceptionally healthy man; no serious illness. Moderately hard worker. Moderate in use of alcohol. Excessive tobacco chewer and smoker. Weight dropped 30 pounds during the past year. One year ago had a severe attack of diarrhea lasting two weeks. Lost weight rapidly during this period and became very weak, so that he was hardly able to stand. No blood noticed in stools. Has had other attacks since, but not so severe. Has had stomach trouble for past six years,—inability to digest food properly. Vomiting has occurred at intervals, but has not been a pronounced symptom. No hematemesis. Appetite fair. About one year ago tongue became very red and raw and very sore.

Present Illness.—Exact date of onset not known because the past illness merged into the present condition. In the early part of the past summer went to the seashore to improve his health, but became very weak while there, being hardly able to move about. Returned after a month unimproved. Has been confined to bed since. Is very weak, cannot digest food, and has much distress after eating. Vomits occasionally; no blood. Is troubled much with dizziness. Has had diarrhea for past two weeks, with semifluid stools; no blood noticed. Sweats profusely at night and has disturbing dreams. Hands cold and clammy. Is short of breath on exertion. Has noticed no hemorrhages in skin or from gums.

Physical Examination.—Patient is of moderate height, with well-developed but soft and flabby musculature. Fairly well nourished; no emaciation. Panniculus present. Color a peculiar lemon-yellow tint. Lips and conjunctivæ pale. Tongue clean. No edema of feet or legs. Pulse 88. Temperature subnormal. Respiration normal. Pulse soft, easily compressible, and regular. Wall not palpable. Lungs clear on auscultation and percussion. Cardiac impulse not seen, but felt in the fifth interspace, 12 cm. from the midsternal line. Dullness not increased to right. Systolic murmur heard all over precordium and transmitted to axilla. Other sounds clear. Liver and spleen not palpable. Stomach not enlarged; no tenderness; no mass felt.

Abdomen not tender; no masses; no dullness in flanks. Ewald test-breakfast: Free HCl 0, total acidity 14, lactic acid 0, pepsin 0. No obstruction. Urine negative.

Feces, no occult blood, mucus, parasites, or ova.

Blood: Hb. 55 per cent.; reds 1,200,000; whites 6000. Micro- and macro- cytes. Marked poikilocytosis. Normoblasts present.

Sept. 22, 1906.—Hb. 40 to 50 per cent.; reds 736,000; whites 2200. Megaloblasts present.

Oct. 11, 1906.—Hb. 45 per cent.; reds 864,000.

Oct. 24, 1906.—Pleurisy with effusion in right chest. Hb. 40 per cent.; reds 1,120,000; whites 4800.

Nov. 15, 1906.—Hb. 55 per cent.; reds 1,750,000; whites 5000.

Dec. 8, 1906.—Hb. 65 per cent.; reds 2,240,000; whites 3000.

Jan. 9, 1907.—Much better; up and about every day. Gained 10 pounds in weight. Tongue sore; is slightly swollen and appears edematous. Lungs clear. Hb. 60 per cent.; reds 1,952,000; whites 8000.

Feb. 28, 1907.—Much weaker. Stomach trouble has returned; gas and pain after eating. Bowels very irregular, with periods of diarrhea. Night-sweats. No loss of weight. Edema of feet and legs at night. Hb. 39 per cent.; reds 1,696,000.

April 27, 1907.—Hb. 26 per cent.; reds 960,000; whites 3000. Micro- and macro-cytes; erythro- and megalo- blasts. Is very pale. Weight remains about the same. Edema of feet and legs at night. Short of breath.

August, 1907.—Effusion in chest returned on opposite side. In bed; very weak. Hb. 35 per cent.; reds 2,600,000. No nucleated cells in smears.

Jan. 13, 1908.—Feeling well recently; some shortness of breath on exertion. Hb. 60 per cent.; reds 2,600,000.

April 22, 1908.—General appearance good. Pruritus of general distribution. Hb. 70 per cent.; reds 2,272,000. No nucleated cells in smears.

From September, 1906, until April, 1908, the treatment with sodium cacodylate was given without remission. The dose at the start was ½ a grain hypodermically, which was increased to 1 grain given every three days. Dr. Kirkpatrick, who carried out the treatment, says that he believes that the success attending this case was due to the sodium cacodylate, as no other specific medication was attempted at any time. No untoward symptoms were noted by him.

The patient has made constant and steady general improvement, and is able to attend to his work.

I have records of 410 cases of simple anemias treated by myself and by others, and in every uncomplicated case there has been complete recovery. I have yet to see a case of anemia in which the administration of this salt has not markedly and usually quickly increased the percentage of hemoglobin and, as a rule, the red cells.

The most brilliant results have been in neuroses accompanying anemia:—

In December, 1910, I treated a young married woman, aged 23 years, whose blood showed 60 per cent. of hemoglobin and 3,600,000 red cells, and who came to me for persistent headache, from which she had suffered for eleven years and was rarely free, the attacks lasting five and six days with but short intermissions. She was given in all 26 injections, commencing with 0.2 Gm., which was continued for two weeks, and then 0.3 Gm. She received in all 6.4

Gm., and was discharged as cured at the end of forty-two days. Since her discharge on March 25th last, she has had no return of the headache.[4]

On February 7, 1910, I commenced treatment of a woman past 30, married, and with 1 child, who gave a history of headaches so severe that at least one-half of her life had been spent in bed, and which were only partly relieved by the persistent use of headache powders containing acetanilid. She reported having been treated by many men of note in various cities, but without avail. Unfortunately no blood examinations were made, but she gave in the color of her skin and mucous membranes every evidence of anemia. Her treatment was carried out in the same manner as in the preceding case, and in all she received 12.5 Gm. Since her discharge on May 2, 1910, she has had but 3 headaches, of short duration.

A case of chronic bronchitis and spasmodic asthma of sixteen years' duration, treated for a mild grade of anemia, was discharged with entire alleviation of the symptoms nineteen months ago, the patient having gained 42 pounds, which he still retains, there having been no recurrence.

My records show 22 cases of neuritis treated, with 16 recoveries. One case of tic douloureux of six months' duration recovered; another improved and then was not benefited. Of 17 cases of eczema, most of them of a squamous type, 15 were cured.

Twenty-two cases of psoriasis were treated, with but 9 recoveries, and several apparently aggravated. Neuralgias and gastralgias responded favorably in almost every instance, and many cases of dysmenorrhea in the evidently neurotic were cured, although in several instances there were recurrences requiring further treatment. Certain types of malaria, such as are seen in former residents of tropical and semitropical regions, which had resisted the persistent use of the quinine salts, gave the most remarkably quick and permanent response.

Sodium cacodylate has proved much more satisfactory in the treatment of chronic rheumatism than other forms of arsenic, and 1 case of rheumatoid arthritis has apparently been checked by its use. A case of puerperal eclampsia has been reported in which there was marked and rapid recovery following its use, but I am not prepared to say that its employment was the cause of this result. As was noted in our previous paper, it was successfully employed in splenic anemia, chorea, and in 1 case of lichen ruber.

It is most important in the administration of the drug that a perfectly pure salt, free from arsenous oxide (As_2O_3) contamination, should be secured.

My present method is to have the pharmacist weigh out for me a number of doses—0.1 Gm., 0.15 Gm., 0.2 Gm., and 0.3 Gm.—and place them in sterile ½-dram phials, tightly corked. This protects this most hygroscopic drug from the effects of the atmosphere. At the time of injection the dry salt is emptied into the barrel of the sterile syringe, into which boiling water is drawn until all the salt is dissolved. As soon as the solution is cooled to about

[4] The notes and the history in this case were reported by Dr. H. W. Carey, of Troy, New York.

body heat, the needle is quickly plunged deeply into the muscle of the buttock, which has been previously sterilized, and the solution slowly injected. No stock solution should be prepared, as it quickly deteriorates; it not only develops fungi, but decomposition takes place, and the amount of sodium cacodylate in each dose is uncertain.

I have established, for my own convenience, an arbitrary and somewhat hybrid standard of 1 mg. for each pound of body weight to start with, gradually increasing the dose to 0.2 Gm., and frequently to 0.3 Gm., and I am sure that the failures to get results with sodium cacodylate are more often due to insufficient dosage than to any other cause.

It would appear that sodium cacodylate is of use in the same class of cases as arsenic, and, because of its non-toxicity, far more desirable in many cases where large dosage is indicated.

I have purposely left any reference to the use of sodium cacodylate as a substitute for dioxydiamidoarsenobenzol until the last, as our knowledge is so limited and the reports so contradictory. It has seemed to many clinicians that, if dioxydiamidoarsenobenzol in large doses were of value in lues, theoretically sodium cacodylate, being less toxic and having a slightly larger percentage of arsenic, should be of value. That this reasoning is fallacious is very tersely stated by Nichols,[5] who says:—

"For all practical purposes dioxydiamidoarsenobenzol should be regarded as a new substance and not merely as a new arsenical compound. The arsenic is only a part of a complicated instrument and would be of little value alone. The arsenic must be reduced, trivalent, and in firm combination with the benzol ring, and the benzol ring must be substituted with the OH group and the NH_2 group in the orthoposition before a maximum destruction of spirochætæ is possible. From this point of view, sodium cacodylate has no more relation to dioxydiamidoarsenobenzol than a pair of artery forceps has to a lithotrite in the extraction of a stone from the bladder."

Since December, 1910, I have received reports on the use of sodium cacodylate in various forms of syphilis from many observers, and many cases have been reported in the medical journals. While in some cases satisfactory results seem to have been obtained, the greater number of observers report it to be of no value, and I am inclined to think they are correct.

If it is used, however, I think that massive doses, such as 0.6 Gm., should be employed, in order that the spirochetes may be overwhelmed, if possible, as is the case with the Ehrlich remedy.

DISCUSSION.

Dr. J. Blake White, New York: This subject is interesting from two points of view: first, that the dosage must be gradually increased, and, second, that whether the greatest good is achieved depends on the manner of administration of the remedy. For obtaining prompt and sure results the hypodermic method is the only true way. With regard to the solutions used, I think, with Dr. Dawes, that they ought to be prepared extemporaneously, as a rule; but there are instances occurring in every one's experience where an emergent demand renders it an advantage to have them already prepared. Therefore, remedies put up in sealed vessels are most useful, and when

[5] Nichols, H. J.: Journal of the American Medical Association, Feb. 18, 1911, p. 494.

they come in ampoules, carefully prepared as to dosage and ready for use, such preparations fulfill a satisfactory purpose. We all know how valuable arsenic is. It increases the red blood-globules, establishes a better relation between the white and red corpuscles, and acts as a valuable eutrophic. I have found that hypodermics of arsenic act very well in certain cases in combination with other remedies.

Dr. Blackader: This is a capital way in which to present a subject. Three or four years ago Dr. Dawes gave us a carefully prepared statement of the physiological action of sodium cacodylate, and now he presents us with the clinical reports of a large number of cases which have been treated with it. I desire to congratulate Dr. Dawes on the excellent work he has done in regard to a remedy which has shown a tendency to fall into disrepute. I feel sure from my own experience with the drug that we have in sodium cacodylate a drug which will give us in many instances results differing from and in some respects more powerful than those which can be obtained from the inorganic salts of arsenic. I also will say that from our own work in Canada I can quite corroborate the statement that sodium cacodylate will not take the place of Ehrlich's new remedy, which is unrivaled in its special field.

Dr. Gordinier, Troy, N. Y.: I have been very much interested in the use of sodium cacodylate for the past two years, and have observed remarkable results in the relief of tabetic pains from its intramuscular injection.

Dr. Dawes: As to the question Dr. Blackader brought up, of the drug's not being considered of value, this is due simply to the *assertion* of T. R. Fraser, of Edinburgh, based upon nothing but an opinion, not upon physiological experimentation. Everywhere that you find anything in the literature as to the statement of the non-value of sodium cacodylate, you will find Fraser's article quoted. He argued that, inasmuch as sodium cacodylate produces no toxic effect on the organism, it cannot be physiologically active. These same statements of Fraser's are being quoted today and taken as the basis for the contention that sodium cacodylate has no effect.

THE USES AND LIMITATIONS OF GENERAL ANESTHESIA PRODUCED BY SUBCUTANEOUS AND INTRAVASCULAR INJECTIONS.

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For certain operations and for certain patients anesthesia by inhalation is undesirable. For operations in the vicinity of the upper respiratory passages, and in certain operations in which the patient is placed in the prone position, anesthesia by inhalation may be either inconvenient or it may interfere with the work of the operator. Again, for certain patients it is desirable to produce unconsciousness without the patient's knowledge that anesthesia is being induced, while diseases of the respiratory system frequently contraindicate irritating inhalations.

For these and, perhaps, other reasons, a number of attempts have been made to produce general anesthesia in other ways than by inhalation. A year had not elapsed after Morton's famous demonstration of ether anesthesia before Pirogoff had produced anesthesia by the introduction of ether vapor into the rectum. Rectal anesthesia, although revived from time to time, has never become popular, since it is difficult to manage, irritating to the intestinal mucous membrane, and tends to produce undesirable distention of the bowel, and at times even death through the rupture of a previously unrecognized intestinal ulcer.

Another method of inducing general anesthesia, also not new, is by intravenous injection. In Bier's method a segment of the limb is anesthetized by isolating it with Esmarch's bandages, and there is introduced into a vein from 40 to 80 c.c. of a ½ per cent. solution of para-aminobenzoyldiethylaminoethanol hydrochloride in physiologic salt solution. This anesthesia, however, and its modification by injecting similar solutions into the arteries of the limb produce only regional anesthesia, and, therefore, will not be considered in this communication.

In an attempt to produce general anesthesia by intravenous injection, quantities of cocaine solution have been injected into the veins, and, while some degree of general anesthesia has resulted, there is no evidence that this is either a safe or a practical method. In 1874 Oré, of Bordeaux, announced a method of general anesthesia produced by injecting a 35 per cent. watery solution of chloral hydrate into a vein of the arm. The dose was regulated by the symptoms induced. It was asserted that the method was superior to the inhalation of ether, as there was no preliminary excitement or after-nausea or vomiting. The fact that the anesthesia was of short duration, that it produced dyspnea, irregularity of heart action, and even fatal syncope, and that

albumin and blood appeared in the urine after the injection were sufficient to cause the method to be abandoned.

In 1909 S. Burkhardt[1] reported his experience with an anesthesia produced by the intravenous injection of watery solutions of ether. A 5 per cent. solution in physiologic saline solution was recommended, 7 per cent. solutions of ether causing evidences of renal irritation. Solutions of chloroform were likewise found to be too irritating. The solution, warmed to 82.4° C., is introduced by means of a suitable needle into one of the prominent veins of the arm. The odor of ether soon appears upon the breath; in some patients excitation occurs, and more rarely bronchial râles.

Usually there is no secondary vomiting or other disagreeable sequela. The dose required is from 200 to 250 c.c. in children, for women 320, and for men 500 c.c. In one case 2500 c.c. were employed. In a certain percentage of the cases the reflexes were not abolished. With the production of full anesthesia the tube is clamped, interrupting the flow of ethereal solution, and as the reflexes reappear from 30 to 70 c.c. more of the solution are introduced. In some patients the anesthesia was continued for as long as one and one-half hours. Objections to the method include sudden death, as reported by Bikin, whose sixteenth patient four minutes after the entrance of the ether solution became pale; the respiration ceased, the pulse dropped to 40, then the heart stopped beating, and, despite artificial respiration and cardiac massage, the patient died. This patient was a poorly nourished woman of 62 with arteriosclerosis and a carcinoma of the mouth. Kuttner in 23 cases found evidence of pulmonary embolism in 2, which fortunately were not fatal. It is evident that thrombi frequently form in the vein about the needle-point, interfering with the injection and raising the danger of embolism. To avoid the objections produced by the high volatility of ether, solutions of hirudin and methylpropylcarbinolurethane have been tried. Sidorenko reports 60 cases of the latter form of anesthesia, a 7.5 per cent. solution of the drug, in physiologic salt solution, being used at a temperature of 40° C.; Fetteroff, of St. Petersburg, also reports 22 cases. Evidences of anesthesia appear in from three to five minutes after beginning the injection, and the anesthesia reaches the periphery in about fifteen minutes. From 250 to 500 c.c. of the solution, and rarely as much as 1200 to 1500 c.c. of the solution, may be required. The best results seem to be obtained when from 50 to 60 c.c. of the solution enter the vein each minute. In several instances there were evidences of thrombosis in the central end of the vein injected. It is apparent that grave dangers attended the injection of such chemical solutions into the circulating blood-stream, and, as thus far developed, intravenous anesthesia cannot be commended for general use.

Although the anesthesia produced by subcutaneous injections is slower in appearing, it avoids many objections of the intravascular anesthesia and is a far safer method. The method is but a development of the narcotic anesthesia as produced by various ancient peoples. The substances injected include chiefly alkaloids derived from opium and various solanacea—morphine, apomorphine,

[1] Münch. med. Woch., Nov. 16, 1909.

hyoscine, scopolamine, and atropine. Subcutaneous injections of chloral have also been successfully used, but this drug is too irritating for subcutaneous use. The conjoint employment of chloral or related chemicals and of alcohol or ether by mouth or by rectum may be useful in intensifying the anesthesia. The safety is increased by securing the cross-action of a number of narcotic and anesthetic drugs. It is first to be noted that hyoscine and scopolamine may be used interchangeably, and that they are of little value in persons under 30, as in young persons the delirifacient action predominates, while in the elderly or debilitated the hypnotic action is evident.

We have employed narcotics to aid the production of anesthesia in over 2000 cases. In some cases narcotics have been used to aid the anesthetic action of ether or that of spinal anesthesia, while in not a few cases the subcutaneous injection alone, or the injection reinforced by the administration of alcohol or Hoffman's anodyne, has been used exclusively for the production of anesthesia. Our observations have proved that satisfactory surgical anesthesia may be produced in selected cases by narcotics alone, but the administration requires considerable judgment, and the technique must be varied according to the age and peculiarities of the patient. Some years ago at the Samaritan Hospital we used no other anesthetic, except in children, for a period of nearly one month, and found it possible satisfactorily to anesthetize, without inhalation, 30 per cent. of the patients that came to the operating table. About 30 per cent. more were anesthetized sufficiently to enable the operation to be done, but the reflexes were active, restraint was required, and the operation was performed under greater difficulty than if ether had been employed. In from 10 to 20 per cent. of the patients excitement and delirium, attended by marked struggling, made it difficult to carry out the operative procedure. In reviewing these cases it was found tha the aged, debilitated, and cachectic were very susceptible to narcotic anesthesia, while the young and robust were resistant and showed a tendency to become delirious. By selecting patients from the former class only we were later enabled to produce satisfactory anesthesia without the additional use of ether or chloroform. For younger patients it was necessary to modify the technique, and in these the delirifacient action of hyoscine or scopolamine was found undesirable, and alcohol and apomorphine, of great value.

On account of the muscular rigidity, except in patients with very relaxed or distended abdomens, none of these methods is well suited for celiotomy. It was also found difficult to abolish the reflexes for rectal operations and to a lesser degree for operations upon the hands or feet. For operations upon the brain, skull, face, jaws, neck, respiratory system, and spine the method is very satisfactory, and often gives results superior to those we have obtained by any other form of anesthesia. After experimenting with various alkaloids, including daturine, hyoscyamine, apocodeine, codeine, and extract of mandragora, it was finally decided that the most important drugs were hyoscine or scopolamine, which are probably identical, morphine, apomorphine, and alcohol or compound spirit of ether. These drugs are employed in combination, according to the peculiarity of the special case, and we now find that one may produce anesthesia

in most persons above the age of 18 without resort to the inhalation of ether or chloroform. By using several of the drugs at one time one may secure a crossed action upon the central nervous system, accentuating the narcosis and reducing the danger to the patient.

The following methods are feasible:—

(*a*) *Alcohol-apomorphine Narcosis.*—My attention was directed to the remarkable sedative influence of apomorphine in patients under the influence of alcohol some fifteen years ago. At this time a young man had been brought to the hospital with lacerated and contused wounds of the scalp who, in his acute alcoholic excitement, was combative and refused to allow his wounds to be sutured. I administered $\frac{1}{10}$ grain of apomorphine subcutaneously for its sedative effect, but found that the patient within a few moments was so insensitive to pain that he made no movement while the wounds were prepared and sutured. The surgical anesthesia, accidentally obtained in this patient, we have, during recent years, deliberately produced. As a rule, it is not convenient or desirable to produce intense alcoholism, and by the conjoint use of morphine the quantity of alcohol may be diminished. The method consists in giving sufficient diluted alcohol or strong spirit by mouth or by rectum to produce alcoholism and then to inject under the skin from $\frac{1}{15}$ to $\frac{1}{7}$ grain of apomorphine, according to the vitality and susceptibility of the patient. In from three to fifteen minutes, if the dose has been sufficient, after a brief and often ineffectual effort at emesis, the patient becomes relaxed, apparently insensible, and may remain in this condition for two or more hours, during which time various operative procedures may be carried out. It must be emphasized that the predominant action of apomorphine is sedative and hypnotic. The emetic action, although it occurs early, is secondary and has been overemphasized. The rather prevalent advice to use apomorphine as an emetic in narcotic poisoning is one of the terrible, if not criminal, errors that has crept into therapeutic teaching. There is, perhaps, no more powerful adjuvant to the action of other narcotics, and a narcotized patient, having been given this drug, frequently entirely fails to vomit as the rapidly increasing narcotism produced by apomorphine overcomes him. Those who carefully watch the effects of apomorphine as an aid in the production of narcotic anesthesia will join me in solemnly warning the profession against the use of this drug as an emetic in any form of depressive or narcotic poisoning.

(*b*) *Scopolamine-Morphine Anesthesia.*—Schneiderlin's revival of the ancients' method of producing surgical anesthesia has met with disfavor, first, because it has been unskillfully used and, second, because it is only well adapted to certain classes of patients. The modified technique we have found efficient is as follows: One and one-half hours before the time of operation, the patient, previously prepared by baths and laxatives, receives a hypodermic injection containing morphine sulphate, $\frac{1}{6}$ grain, with hyoscine or scopolamine hydrobromide, $\frac{1}{100}$ grain. Twenty minutes later the patient's condition is carefully observed, the injection is repeated, and immediately afterward there is slowly run into the bowel an enema consisting of Hoffman's anodyne, 1 ounce; alcohol, ½ ounce; physiologic saline solution, enough to make 5 ounces.

The patient is now continuously watched and the character of further injections determined by studying his susceptibility. Twenty minutes after the second injection, if the patient be old or debilitated, sufficient narcosis may have been induced so that he cannot be roused by shaking, shouting, or pinching, and is, therefore, ready for the operation. More frequently the patient is somnolent, but may be partially aroused. In such a case, if the pulse is good, a third injection containing apomorphine hydrobromide, from $\frac{1}{20}$ to $\frac{1}{10}$ grain, according to the strength of the patient, is administered. In still other cases the patient is quite wakeful, and shows only the more superficial degree of narcosis. In this event the third hypodermic may consist of morphine sulphate, $\frac{1}{6}$ grain; scopolamine or hyoscine hydrobromide, $\frac{1}{100}$ grain, and apomorphine hydrochloride, from $\frac{1}{20}$ to $\frac{1}{10}$ grain. If the patient shows a red, flushed skin, if the pupils are more or less dilated, and if there is delirium, the hyoscine or scopolamine is omitted, and the morphine and apomorphine used. On the other hand, if the pupils are small, the respiration slow, and the face rather pale, although the patient is not sufficiently narcotized, the morphine should be omitted from the third injection and the hyoscine or scopolamine used. If the heart action is weak, or if the patient is greatly debilitated, the apomorphine, which is the most powerful of the agents employed, must be avoided or used with caution. If the patient be above 40 years of age, and especially if the patient be debilitated or toxemic, in from ten to twenty minutes after the third injection, if not before the third injection, profound narcosis will be present. The effect of the apomorphine often comes on with startling rapidity. The patient who has been stupefied by the previous injections may within two or three minutes after the injection of the apomorphine raise the head, or the hand to the mouth, as if nauseated, and without vomiting instantly fall back entirely insensible, so that the most extensive operative procedures may be begun at once.

It is to be observed that the patient is to be constantly watched while under narcotic anesthesia, just as a patient is to be watched while under ether anesthesia, and that the induction of the anesthesia by the use of repeated doses, selected according to the patient's susceptibility and the effects desired, corresponds to the work of the etherizer, who drops the anesthetic upon the gauze or withholds it, according to the condition he observes in the patient. In some cases a fifth injection may be necessary, either before the operation or during the course of some very prolonged operative procedure. The duration of the narcosis is from two to eight hours, and the patient usually awakens with no recollection of having fallen asleep or of having awakened, and not infrequently at once begins to inquire as to when the operation is to be performed.

By this method we have narcotized patients in their homes and have had them conveyed unconscious to the hospital. One patient, after an excision of a carcinoma of the parotid, was reconveyed back to her home, and there awakened some hours later entirely ignorant of the fact that she had left her bed. In this manner I have also operated upon patients who were either delirious and fought against the operative procedure or in whom it was desired to operate

without the patient's knowledge that an operation was to be done at the particular time. Thus, those patients who have desired operative treatment, but who have refused through fear, cowardice, or mental perversion, have been successfully and unconsciously subjected to operative treatment. For some years we have performed nearly all craniotomies and operations upon the brain and cord upon patients over 35 years of age with this form of anesthesia, excepting in those patients who were comatose from injury. Likewise, extensive plastic operations upon the face, resections of the jaw and tongue, and many of the operations upon the pharynx and larynx have thus been performed. The method is also very valuable for operations upon the thyroid. A narcosis sufficiently incomplete, so that the patient exhibits a slight muttering delirium, is useful in operating in the region of the recurrent laryngeal nerve. We have also obtained very satisfactory anesthesia in younger patients by this method in those cases where well-marked debility or asthenia was present. Thus we obtained an intense narcosis in a boy of 16 who had a large postpharyngeal fibroid tumor.

(*c*) In persons under 30 the *combination of methods a and b* is often desirable. The scopolamine and hyoscine are to be used cautiously and omitted if too marked a delirifacient action is observed, while full doses of alcohol, morphine, and apomorphine are often requisite.

Precautions.—The respiration and pulse should be constantly watched while the patient is under narcotic anesthesia. As the method produces respiratory depression, it should be avoided where there is marked depression of the respiratory centers or disease abolishing to a large degree pulmonary function. In conditions of profound toxemia, as in sepsis or advanced renal or hepatic disease, there may be danger in increasing the pre-existing toxemia, and the narcotics should be used very cautiously or not at all. Patients with tuberculosis or moderately advanced carcinoma are often unusually susceptible and usually are good subjects. Obviously, it is not a method to be used upon patients who are near the point of death from some hopeless disease.

At the completion of the operation 2 quarts of salt solution are run into the bowel to aid in the elimination of the drugs. If the narcosis is excessive, 3 to 5 grains of caffeine, with from $\frac{1}{20}$ to $\frac{1}{10}$ grain of strychnine, are to be given subcutaneously, and an enema containing 1 pint of black coffee and 2 drams of tincture of capsicum in 1 quart of hot water is also administered. If cardiac failure or collapse occurs, the intravenous injection of a pint of physiologic saline solution containing 5 minims of adrenalin is probably the most powerful known means of cardiac stimulation. No incision is required, a sharp needle connected with a suitable funnel or burette being thrust into a vein in the arm. More important, and to be doubly emphasized, is the maintenance of the patency of the upper air passages in narcotic, as well as in other forms of, anesthesia. I am convinced that in many cases patients have been permitted to suffocate, the tongue having fallen back into the throat, and the movements of the muscles of respiration having suggested to the physician that breathing was being continued. Especially is this important after operations upon the tongue or floor of the mouth. In one of my patients, after excision of one-half

of the tongue, not less than two residents saw the patient and ordered stimulation, but permitted the patient slowly to suffocate to death. In several other cases I have seen patients nearly die because the resident or nurse diagnosed collapse, and refused to believe, even when told, that there was respiratory obstruction—whereas all that was required was the holding forward of the tongue or of the lower jaw. I now insist that respiratory function shall be determined not by the movements of the neck, chest, or abdomen, but by the movements of a wisp of cotton placed over the mouth or nose, and that in all cases of narcotic anesthesia any sudden change in the patient is to be first treated by the holding forward of the tongue or lower jaw. It follows that in profound narcosis liquids must not be placed in the mouth. While a student I saw a case of opium poisoning in which strangulation and death soon followed the pouring of stimulants into the mouth.

The patient under narcotic anesthesia, like the patient under other forms of general anesthesia, must be continuously watched by a competent person from the time the first injection is given until the anesthetic has passed off. In the hands of the careless or incompetent it is a method too dangerous ever to be employed. I know of two asthenic alcoholics who came into the receiving room of the hospital some years ago with delirium tremens. Something between $\frac{1}{10}$ and $\frac{1}{5}$ grain of apomorphine was ordered by the resident in each case. They were left alone, and, not long after, both patients were found dead. It seems to me that each patient became asphyxiated under the narcosis of apomorphine. Ether narcosis develops during the administration of the drug; narcotic anesthesia, some time after. The induction of the one should be as carefully watched as that of the other.

Respiratory Depression.—Twice I have seen the respiratory rate reduced to three or four per minute. In neither case did harm result. The first patient promptly awakened and resumed a more normal respiratory rate when an attempt was made to introduce a catheter. Despite the shallow and very infrequent respirations there was no cyanosis or pallor, and the pulse remained good. In the second patient the normal rate of respiration was gradually resumed, enemas and hypodermic injections being used to aid in the elimination of the narcotic.

Finally, it is to be remarked that there is no universal anesthetic, nor has the ideal anesthetic been discovered. Ether is and will remain the most generally used of all the anesthetic drugs, but local and spinal anesthesia, we believe, each have a distinct sphere of usefulness. Likewise, narcotic anesthesia is useful for certain operations upon the upper part of the body under especial conditions where general, spinal, or local anesthesia is inapplicable or objectionable. When properly employed, and for selected conditions, this method of anesthesia is as yet unsurpassed, and from the patient's viewpoint is nearly ideal.

DISCUSSION.

Dr. A. Ernest Gallant, New York: I do not know whether it is fair to discuss a method one has not used, but it may be justifiable to present our experience in similar directions until we try the method. I have had no experience with injecting ether into the veins, and I have not tried to operate with a combination of morphine and scopolamine constituting the sole anesthetic, because I have always used chloroform

or ether in conjunction with these drugs. The remarkable thing is to see the patients who are anesthetized in this way. I remember once I was delayed after a dose of morphine had been given hypodermically, so that it was four hours before I began operating. The patient was spoken to, walked out of the room, and lay down on the table, and the next day, when she was conscious, we asked her what she thought of that dream. She said she had not been conscious after the nurse stuck the needle in. I could probably have performed the operation without the woman recoving consciousness. Among my patients I have but few alcoholics to deal with, but I regard apomorphine highly as a sedative. It has a good effect in a sedative way; therefore, I think that what Dr. Babcock says about it is true. As to the effect of bromide, I know it will not exert as much benefit as one or two doses of apomorphine. Of course, in the method the doctor presents there is no question about the fact that the dose is the important thing. It must be in proportion to the weight of the patient; one must measure the dose and watch the patient, and it is a question of good judgment and experience. One cannot do anything without securing a condition of muscular relaxation. As to the danger of suffocation, I think that the doctor's trouble is with the tongue; the danger point is first due to the neglect on the part of most anesthetizers to see that the head is lifted forward and high enough. When during anesthesia the head is permitted to drop backward so that the cervical vertebræ arch forward and the root of the tongue drops backward, serious obstruction to respiration must result. On the other hand, when the head is fixed forward, with the chin close to the sternum, so that the cervical vertebræ form a concavity, enlarging the nasopharyngeal space of its maximum, the root of the tongue is drawn forward and cannot interfere with respiration.

Dr. Blackader: I think we must not lose sight of the fact that at the present time the safest form of anesthesia is that induced by ether given through the respiratory tract, although this may be supplemented, under special circumstances, by the previous hypodermic introduction of modifying hypnotics, such as morphine and scopolamine or hyoscine, thus rendering a smaller amount of ether necessary, and facilitating its administration. The objection to these mixed anesthesias is the interference with danger signals which may take place. If we come to actual statistics, I question whether any of these newer methods of anesthesia will give a safer anesthesia than can be obtained under ether given by the drop or open drop method. We, as an association, must be very careful in our recommendations of the newer methods until we know more about them. Such methods as those recommended by Dr. Babcock may be undertaken in large hospitals where we have every kind of aid at our hand; but should rarely be employed in private practice.

Dr. Babcock: I wish to thank you, gentlemen, for your discussion of the paper and for the additions that you have made to it; additions that I fully endorse, but did not mention on account of the limitation of time. For general and indiscriminate use I consider ether the safest anesthetic. These special methods require special conditions. Often the special method becomes valuable because the conventional anesthetic is in the particular case dangerous. Thus, for operations upon the larynx or upper jaw the danger of aspiration pneumonia and the frequent necessity of an additional tracheotomy render the use of ether especially hazardous, while narcotic anesthesia is relatively convenient and safe. As therapeutists, we should take a broader view of the subject of anesthesia. A trained anesthetist should have a far wider knowledge of anesthesia than that embraced in the action of ether alone. By being able to select the appropriate anesthetic for the particular case, be it nitrous oxide, ethyl chloride, cocaine locally, ether, chloroform; rectal, spinal, or narcotic anesthesia, not only can many unpleasant features incident to operations be ameliorated, but the mortality of the operations can be distinctly reduced. This paper is offered, therefore, not merely to present the subject of a special form of anesthesia, but to aid in stimulating a broader study of the entire subject.

HYPODERMIC MEDICATION; ITS ADVANTAGES AND TECHNIQUE.

Abstract of Paper
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It was not the intention of this paper to add to our knowledge of this subject, but rather to emphasize the value of a more general use of the hypodermic method and promote a proper recognition of the various details essential to success in its practice. These, as all knew, were too frequently disregarded, a neglect which resulted in detriment to the patient, if not in effects that greatly detracted from the usefulness of this system of treatment. The paper no doubt would appear rather elementary to those who regularly practised subcutaneous injection, but there were others to whom these details might naturally seem not to be of sufficient importance to warrant the very careful attention which they really required. If one paused a moment for reflection one would see that all the most certain results obtained today with therapeutic agents were achieved through this method of applying them, and it were natural to suppose that this already wide field would in the future be still further developed and enhanced in value. The paper included detailed directions in regard to the proper technique to be followed in making hypodermic injections.

DISCUSSION.

Dr. Dawes: Dr. White may practically be considered the father of this method in the present generation. Certainly, he has had more experience with it than others. Personally, I am a very strong advocate of the hypodermic method not only for sodium cacodylate, but for other drugs. In teaching our students we say that we get a better effect—a more exact effect—where we do away practically with what we call, for lack of a broader name, "idiosyncrasy," and instead of introducing into the individual stomach a drug without knowing how it is to be eliminated, or what its effect, we get a definite and dependable effect by using the hypodermic syringe. We say all this and then proceed to go out and give our drugs in pills or capsules; so that our position is certainly anomalous. Wherever I can, I use the hypodermic method, and it is not really so difficult to get your patients to let you administer drugs in that way. You only have to use one or two injections a day, where by the mouth you might have to give five or six doses, and at least twice the amount of drug. My method is to introduce the remedy intramuscularly, instead of subcutaneously. Meltzer and Auer have shown that the drug is absorbed more rapidly if given intramuscularly than if given subcutaneously, and my own clinical experience is in line with this. Another point is to have the temperature of the injection as near to the body temperature as possible (and Dr. White spoke of that) not only because it is absorbed more rapidly, but because there is less discomfort to the patient. In regard to large doses of sodium cacodylate, if you want to administer 600 mg. you should give two injections, as the result will be that the patient will refuse to take the treatment if you give such large single doses, on account of the pains produced. I think that we, as a society, ought to encourage the use of the hypodermic syringe as much as possible.

Dr. Robert T. Morris, New York: There is one side of this subject that surgeons would like to hear about. Not long ago I read about a doctor who injected in cases of

chronic syphilis a certain solution which was painful and caused abscesses; but the patients were cured. He said he knew they were cured because none of them came back again for treatment. Two weeks ago I was cabled to go abroad to operate for a stomach ulcer, which it was impossible for me to do, and yesterday I got a letter describing the case. A lad had been given a tonic by hypodermic injection, and the injections had been followed by two abscesses, after which the stomach ulcer appeared. Toxins had probably been absorbed from the hypodermic needle abscesses, and had caused the gastric ulcer while being eliminated.

Dr. Stewart: Some years ago, when I was physician for a New York charitable institution and engaged in calling on patients in the tenement house district, I found it impossible to obtain sterile water for hypodermic medication without carrying a supply with me. I, therefore, conceived the plan of sterilizing the tap water extemporaneously by boiling it in a teaspoon wth the aid of a match. Some years ago, at Dr. John V. Shoemaker's hospital for skin diseases, we tried mercuric chloride hypodermically in treating syphiloderma, but the patients would not come back for a second injection on account of the pain resulting from the injections. We soon found out, however, that the pain was produced by the dull needles used, rather than by the drug employed. So we took care thereafter to use sharp needles; also to sharpen our needles after using this drug, as it corroded the needles. Then our patients came back for further treatment.

Dr. White: In my practice I have substituted the chloride of gold and sodium for mercury salts for hypodermic use, since it is not so apt to cause after-effects, and have found it very satisfactory when thus employed.

ON THE RADICAL REMOVAL OF THE CONDITIONS CAUSING ARTERIAL CHANGES LEADING TO NON-PSYCHOGENIC DISTURBANCES OF THE NERVOUS SYSTEM.

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WHETHER persistent high blood-pressure is itself the cause of arterio-sclerosis or whether it is only another effect of toxicosis which causes degeneration of the arteries is still a problem.

We now know that sclerosis of the arteries occurs in some subjects without a marked rise of blood-pressure (Councilman). It is in these cases that we have to rely upon other signs for a diagnosis, more especially when nephritis has not occurred. It is in the nervous system that these signs reveal themselves earliest; and it is unfortunate that sclerogenetic toxic states are so often overlooked by physicians on account of the facility with which it has been the habit to label "neurasthenia" the varying symptoms in the causation of which circumscribed lesions of the nervous system can be excluded.

It needs to be reiterated that there is no nosological entity neurasthenia, which is only a rather loose name for a clinical condition attributable to some definite cause or causes, generally intoxicative, such as hypo- or hyper- thyroidism, deficiency of the adrenals, incipient Bright's disease, disturbances of the digestive organs, tuberculosis, syphilis, pellagra, or other chronic infections, animal parasites; a poor, badly balanced, or excessive diet; the imbibing of exogenous toxins, and, lastly, mental worry and unhappiness, which act indirectly by perverting metabolism and thus producing the toxicosis which determines neurasthenia.

It is the doctor's business to find out the causes in each case, and to remedy them. In searching for these the general practitioner may require the aid of specialists. This is particularly so where the nervous system is affected; for I am sorry to say that neurological technique has been acquired up to the present by but a very few of the busy men who pursue general or special practice. In illustration of these statements are reported the following cases, in which the gravity of the symptoms led to an early consultation, permitting of the institution of proper treatment in time, with the result that good health was quickly restored:—

CASE I.—A man of 64, chief architect in the Indian Service, consulted me February 10, 1910, having been sent by Dr. Philip Roy because of the recent occurrence of epileptiform convulsions with loss of consciousness.

Previous History.—Scarlet fever at 6, without bad sequelæ. An active, healthy man, except for two years of asthma twenty-five years before—a result of constant attacks of catarrh. It was cured by working as a farm hand for three weeks.

He smokes two cigars and a pipe a day. He took coffee and was a heavy drinker until after the attack; now he has ceased to take even tea. He has always been abstemious in eating, but has been fond of salty foods. He drank "when he felt like it."

The first epileptiform attack occurred in May, 1909, at an elevation of 12,000 feet, near Durango, while he was inspecting the school buildings there. He was unconscious for half an hour. The second attack occurred shortly after, upon leaving a train in Chicago, while making for the staircase. It lasted about an hour. A third attack took place in July of the same year in his office, lasting one and a half hours. The fourth and last occurred two nights before his visit to me, while he was visiting a friend and sitting down. It lasted three hours.

The attacks are preceded by a creeping sensation in the left upper arm, passing slowly down to the hand, which becomes numb. In about fifteen minutes unconsciousness supervenes. The face is said to be flushed; but he is uncertain whether there are convulsions, though others have told him that there are. The duration of the attacks was only surmised.

Since these attacks he has had a pain over the forehead when coryza occurred. As he had read that insanity might come on from this catarrh, he was at first a little anxious about his state; but soon steeled himself against such fear. The pain in the head was rather a feeling of depression and a grumbling pain like that of catarrh. The discharge was slight, and the headache disappeared when it ceased. He used to sleep quite well; but about the time of his attacks began waking in the early morning, and could not fall asleep again. This persisted.

He had been recommended to eat more, and to take fat meat, and this he has done.

Physical Examination.—Blood-pressure 180 mm. Hg. No manifest sclerosis or cardiac hypertrophy. No albuminuria.

Reflexes.—Knee kick, R. > L.; Achilles reflex, R. > L.; Triceps, L. > R. Radials equal. None markedly exaggerated. Plantar reflex is flexor. The left cremaster is absent.

Sensibility.—No abnormality in lower limbs to pain, touch, temperature, or attitudes, though the latter are sometimes wrongly named, but correctly recognized. Arms: Perfect localization of light touches, both segmentally and axially. Spacing sense of fingers normal. Other modalities normal except sense of attitudes poor, especially in the left hand. No hemiopia or color inversion of visual fields.

Motility.—Normal, but left fingers weaker than right. Diodocokinesis regular. Pupils contract promptly.

Psychic Functions.—Thinks his memory has been weakened since the attacks. There are no disorders of speech. Emotionally, he has always been easily excited when there was a cause, and has been accustomed to occasional sadness.

Diagnosis.—The localization of the aura in the left arm and hand, along with the increase of the triceps reflex and the loss of the cremasteric, point to an organic perturbation of the sensorimotor area of the right hemisphere, probably mainly in or near the cortex of the central fissure, opposite the second frontal convolution. The cremaster-governing fibers are, of course, attacked in some other situation.

As neoplasm and granuloma were each unlikely, and as the man's age was that of arteriosclerosis, of the state preceding which the recently acquired matutinal insomnia was indicative, I believed it wise, although lacking proof, to adopt the supposition of sclerogenetic toxicosis, and to put it to the experimental proof of therapeutics. Accordingly, a diet light in proteins was ordered, and coffee and tobacco were forbidden.

The result was confirmatory, as the patient, one year from the consultation, remains free from attacks and insomnia, and is perfectly well able to perform

his very strenuous work, often in high altitudes. His blood-pressure is about 160 mm. Hg.

I believe that the first attack was inaugurated in consequence of ischemia of a part of the right Rolandic region, due to the fact that the heart, strained by the high altitude, was not able to keep full of blood a partially sclerosed vessel distributed to that area. The second attack was likewise due to a sudden demand upon the heart upon leaving the train after a very hot journey.

CASE II.—Physician aged 68, referred to me by Dr. Balloch because of a "nervous breakdown." For over a year, he had been worrying over the death of his son and the serious illness of his wife and daughter. He was suffering from severe insomnia, tinnitus aurium, and numbness and tingling in the toes of the left foot and in the hand; sometimes less markedly in the right. He sometimes lost the ability to distinguish one from two pins between thumb and fingers. His power of endurance and sight and hearing had markedly diminished, and his former optimism had changed into an incapacity for enjoyment. All the organs were normal, but he had lost about twelve pounds, although the appetite was fairly good. He believed that he was not physically ill.

On questioning, it was found that he had slept badly for about five years, waking in the early morning, unless he took diethylmalonylurea, of which he used 5 grains every fourth night. On waking, sad thoughts of his son's death and daughter's troubles made him weep.

Physical Examination.—Reflexes rather active. Motor functions and diodocokinesis well performed. Sensibility normal. Heart normal. Pulse slow and regular. Blood-pressure 187 mm. Hg. Liver rather small. The paresthesiæ disappear when the parts are stretched, and occur only when he worries.

Diagnosis.—Sclerogenetic toxicosis was diagnosed from the raised pressure, the nature of the insomnia, the paresthesiæ without sensory defect, and the loss of endurance.

Treatment.—A low purin and protein diet was prescribed, and hypnotics were forbidden. In a few days he began to feel better, and now, nearly two years later, he remains quite well. He had been taking a popular aromatic caffeine beverage, and this was stopped as soon as I learned of it.

It is not only in the aged that the presclerotic syndrome with nervous disturbances occurs and can be removed by means of a diet low in nitrogen and purins. The following case will illustrate this:—

CASE III.—METABOLIC PSYCHASTHENIA.—An engineer, 38, referred by Dr. Atkinson. A powerful, energetic man, formerly accustomed to active work, he began to be unable to concentrate upon the office work to which he had confined himself for over three months. Previous to this he had been much less active. Lately, too, he had been very much worried by an official inquiry into a contract for which he had been mainly responsible. For no cause known to him, he experienced a feeling of dread in the mornings, and an indecision in business matters was now realized to have been present several months. There was no syphilis, nor any other organic disease.

He had been improved by three weeks in the woods, during which he had been very somnolent, but relapsed at once upon his return, and could hardly stand the morning suffering. There was no insomnia.

Physical Examination.—The reflexes were rather active; but there was no other objective change in the lower neurons. There was no amnesia. The sexual hygiene was normal. He was much depressed, and longed to go away from it all for a year, which he could well afford to do.

Treatment.—He was sent for three weeks into the mountains. This time he fully recovered, on account of the light diet which he took. Breakfast and supper consisted

of fruit and milk, and his midday dinner was of vegetables and 6 ounces of meat; after a few days cereals were added morning and night. He is now at the head of a large business demanding much office work.

Since prevention excels cure, such results are better than those obtained by removal of the effects by baths, electricity, or chemical eliminants (diuretics, sudorifics, purgatives), or antagonists (iodides, nitrites), or, still worse, narcotics, hypnotics, or calmatives, which only mask the disease while it progresses.

The Diet in Arteriosclerosis and in Neurasthenia of the Climacteric.

To prevent the formation of toxins is both easier and more effective than to eliminate them when formed,—though, of course, the latter can be done by stimulating the emunctories of the skin by baths, of the bowel by purgatives, of the kidneys by diuretics, of the lungs by active exercise, or of the whole organism by electricity. The suppression of the effects of toxins by counteracting substances, such as the nitrites or iodides, is still less desirable; and no condemnation is too great for the masking of the warning symptoms through the use of sedatives, such as bromides, or of hypnotics and narcotics, such as chloral, morphine, alcohol, or the synthetic drugs. Another measure to be reprehended is the whipping up of the body reactions by means of the strychnine or caffeine groups of alkaloids.

As the patient's ill health is due to his inability to metabolize the excess of protein which he had formerly taken with relative impunity, the indication is to see that he takes only the physiological amount, which for a person past midlife should not exceed 50 grams per day. At the same time, calories must not be deficient. In the third place, the vegetable salts must be supplied in sufficient amount for free secretory and excretory activity.

Following is a sketch of a suitable diet, which, of course, must be varied to suit individual cases:—

While dressing, 5 to 10 ounces of hot water containing 10 to 20 grains of either sodium sulphate, potassium citrate, sodium phosphate or carbonate, or some similar alkaline or neutral saline, according to the nature of the case. Half an hour later, breakfast, consisting of a *large* plate of fruit and milk or cream, followed by abundant cereal and milk with bread and butter. No meat, eggs, or fish. Wait five hours. Dinner: Not more than 4 ounces of meat or fish, which must be quite fresh; a *very large* plate of green vegetables; potatoes sparingly, and preferably nothing more than perhaps a taste of sweets. The evening meal, five hours later, may be a repetition of the breakfast; but in it succulent vegetables may replace the fruit, and macaroni or a similar dish be substituted for the cereal. Thirst and hunger between times may be satisfied by water and fruit, taken about one hour before a meal or during the night. The purins are to be avoided; therefore, meat juices are abstained from, and soup, which may be taken at dinner or supper, must be made entirely of vegetable food. Alcohol is forbidden, even as beer or wine. Tea, coffee,

cocoa, and kola must be abstained from, since, besides being closely allied to the xanthin bodies, they are toxic to the nervous and circulatory systems.

Gradually this diet is added to, an occasional egg being given at breakfast or supper. The patient very soon learns what suits him best. Some culinary ingenuity is needed to give variety to a diet which at first appears monotonous. In this respect the tastiness of well-prepared whole wheat bread is a great gain.

Gentle and regular *exercise,* twice daily, is a marked aid to healthy metabolism, and proper calmative *baths* are most beneficial. Of course, proper *psychotherapy,* to allay the patient's alarm, is of great importance; besides which, it teaches him the real status of his health, and provides him with the means of counteracting his mental depression by the knowledge that it has a physical source, and will pass away as this improves. Sometimes the morbid depressive ideas are somewhat fixed; and they must then be met by frequent, rational persuasion to readjust the patient's point of view. The effect of a change of environment is often only temporary, unless it be not made merely empirically. If it be made part of a psychological reconstruction and guided by the physician, it should, however, help rather than hinder the resumption of work, even in an unsatisfactory environment.

GENERAL PARESIS, TABES, AND CEREBROSPINAL SYPHILIS.

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Etiology.—In all three conditions we have, as the primary cause, syphilis. In general paresis and tabes no active elements of the primary infection are present, that is, no spirochetæ are found in the diseased tissues. We have rather the effects, probably, of toxins, which manifest themselves in the induction of a fibrosis of the nerve-tissue and blood-vessels. Probably 5 to 10 per cent. of those acquiring syphilis are affected with general paresis or tabes, and a like proportion with syphilis of the nervous system. We should divide these diseases into two classes: (*a*) General paresis and tabes; (*b*) cerebrospinal syphilis. The first class includes parasyphilitic disorders and the second a syphilitic affection of the nervous system. An important feature is the time elapsing between the initial infection and the appearance of the lesions of the nervous system in syphilis and in parasyphilis. In parasyphilitic diseases,—general paresis and tabes,—the disorder rarely shows itself before ten years have elapsed and often still later, while in syphilis it usually occurs within five years.

Other causes are important factors in exciting the diseases under consideration: Injury, strain, overexertion; exhausting diseases, such as typhoid fever, excesses, alcohol, venery, heredity, etc. Perhaps without these exciting agents no involvement of the nervous system would take place; but the converse is still more positive, viz., that without syphilis there would probably be no general paresis or tabes.

Symptomatology.—Between general paresis and tabes there are many points of resemblance, as well as many of difference. As we have seen, these affections occur at about the same time after the primary infection and are both parasyphilitic. Each may present a long prodromal period before the symptoms become prominent. This is, perhaps, more clearly observed in tabes, when carefully investigated, than in general paresis, but even in the latter the history of the disease, before acute mental disturbance develops, will often reveal the fact that there has been some change in character or personality months or even years before, which was not fully appreciated. In tabes there may be a history of pain, or anesthesia, or some slight vesical weakness, or uncertainty of gait which existed a long time before the patient consulted a physician. Probably at the time a careful examination of the pupillary reactions in both diseases would have shown partial or complete Argyll-Robertson pupils. I have seen the Argyll-Robertson pupil years before any of the clinical manifestations appeared. Indeed, I consider this symptom

the most important—the cardinal symptom—in the diagnosis of general paresis or tabes, hesitating without its presence to make a positive diagnosis. In one case where the diagnosis was important from a legal point of view, the mental side was positive; the absence of the Argyll-Robertson reaction, however, led us to qualify the diagnosis and therefore the prognosis; the wisdom of this was shown two years later by the recovery of the patient. The importance of this symptom cannot be overestimated, as its early manifestation gives us the only possibility of cure or stay of the disease by treatment.

The two characteristics just referred to—prodromal period and Argyll-Robertson pupil—are common to both diseases, general paresis and tabes. The other symptoms, while in some degree similar in each, differ so widely in intensity as almost to be different in nature. Many authorities, especially Mott and Ferrier, are very positive that the two diseases are identical, the clinical differences between them being due merely to the situation of the lesion, while the nature of the pathological changes is the same. I think, however, that when we take up the course and symptoms and study them individually the differences will show themselves most markedly.

Confining ourselves to the spinal cord lesion and the cranial nerves, we find, in general paresis, either spasticity and exaggerated reflexes (which certainly are not symptomatic of tabes) or loss of reflexes with ataxia of a mild degree, rarely as extreme as that found in tabes of the typical form. Again, in general paresis we often observe spastic paraplegia and ataxia, representing a combined sclerosis of the spinal cord, as is shown by the pathological changes. In tabes the spinal symptoms are all of the sensory type, as shown in the pains, the paresthesias, and the ataxia or loss of the muscular sense, but never of the motor type,—paralysis, contractures. The latter conditions, when present, are caused by disuse, never by a true lesion of the spinal cord involving its motor or lateral tracts. The terminal stage of tabes, so-called the "paralytic," is a misnomer: There is no true paralysis; there is simply a complete loss of direction of motion.

The sensory side of the disease in tabes is shown by the extreme pain,—not only the lightning-like, stabbing pains of the extremities and trunk, but also the crises of rectal, vesical, cardiac, and gastric origin. These are infrequent in general paresis; even in the so-called "tabetic type" of general paresis they are rarely extreme.

Vesical paresis, so common in tabes, is unusual in general paresis. We must not confuse mental weakness and inattention to emptying the bladder with paralysis of that organ.

We might mention also the joint involvements and the foot ulcers, which, indeed, while not common in tabes, are certainly not present in general paresis.

The cranial nerve lesions, with the exception of the oculomotor, also differ in the two diseases. Optic atrophy is rare in general paresis, and especially is this so in the cerebral type. Affections of the third nerve such as are represented in ptosis and paralysis of ocular muscles, while common in tabes, are rare in general paresis, even of the tabetic type.

No case of general paresis runs its course without spinal cord involvement, probably of both the lateral and posterior columns, but in no case is there such complete involvement of the posterior columns as is seen in typical tabes.

Another important point is the duration of the two diseases. General paresis lasts in a typical cerebral form about three years; in the tabetic and irregular forms possibly five or even ten years; these latter cases are unusual. Tabes lasts ten or twenty years, unless some intercurrent complication, possibly cystitis, abruptly ends the case.

Passing now to the mental symptoms: In tabes, if the affection remains confined to the spinal cord, there are no mental symptoms. The mind is unaffected; the intellect is as acute as at the onset of the disease. If these diseases were really identical, it is not probable that the lesion could remain for twenty years confined to the spinal cord alone. The converse is not true: General paresis always manifests spinal symptoms, unimportant as compared with the mental, but still always present.

The mental symptoms of general paresis are so well defined—grandiose, exaggerated delusions of power, strength, riches, etc., and, in recent years, the depression or dementia even in the early stages—that there is no possibility of mistaking them in our cases of tabes, if present. We do, indeed, find, after many years, mental disturbances in some cases of tabes, as in other chronic diseases, but these disturbances do not present the special characteristics of those of general paresis.

Pathology.—The pathological condition in general paresis consists essentially in an involvement of the cerebral meninges, especially the pia mater, and the cerebral cortex, affecting the cortical cells or neurons. There is also an early involvement of the associative fibers. This explains in part the mental side of the symptoms, *i.e.*, the exaltation or depression and loss of association of ideas. The blood-vessels, when involved, are not occluded by the thickening of their walls, as is frequently the case in syphilis of the brain. The cranial nerves and the spinal tracts are the seat of degeneration. In tabes the initial lesion resides in the spinal ganglion and the neurons of the posterior column lying just outside the posterior gray horns; later the posterior nerve roots and columns are involved. Rarely do we find the lateral columns involved, except in protracted cases, and then only in a limited degree. The cranial nerves are usually involved more extensively than in general paresis. The blood-vessels are narrowed in caliber, and there are degenerative changes in their walls resembling the changes found in general paresis. The distinction in the two diseases is the same as pointed out by Mott and Ferrier, but it is one which remains definite and is valuable as a differential point in diagnosis.

Cerebrospinal Syphilis.—This differs etiologically, clinically, and pathologically from the parasyphilitic diseases, general paresis and tabes. Etiologically we have here the primary syphilitic infection, which directly by its presence, as shown by the spirochetæ, infiltrates the nerve-tissues and blood-vessels, impairs the function, and may destroy the structure, of those elements.

The early involvement of the nervous system—within a few years, even in some cases in a few weeks—is diagnostic of primary syphilis. Some of the

symptoms resemble general paresis and tabes, especially the latter. The pupil is suggestive of the Argyll-Robertson syndrome, being sluggish in its reaction to light. Ocular muscle paralysis is usually present, often evanescent. There may be tabetic symptoms,—loss of reflexes resembling, indeed, tabes,—but their onset has been too rapid to be mistaken for the slow progressive course of tabes. Myelitis is common, or poliomyelitis, generally of the chronic type.

The mental symptoms, especially in alcoholic cases, often make a diagnosis from general paresis difficult. In the typical cerebral cases of general paresis, the course is usually rapid, dementia, convulsions, contractures of the extremities closing the scene. Of late years there seems to have developed a different type of the disease, longer in duration and less marked by exaltation; indeed, depression and early dementia are present. This is more often the case when there are tabetic symptoms, but also occurs when the reflexes are exaggerated from the beginning.

Tabes has not changed in its symptomatology as the disease has been further studied. It is usually a protracted affection, pain, ataxia, vesical weakness, Argyll-Robertson pupils, and other cranial nerve involvement being the rule. The mental condition usually remains uninfluenced to the end.

The course of syphilis of the nervous system, as would be expected from its pathology, presents an entirely different picture. It is manifested in local symptoms, cerebral paralysis, focal epileptic seizures, cranial nerve lesions, transverse myelitis, poliomyelitis, etc.,—conditions not necessarily permanent, as the infiltration may be absorbed.

The *prognosis* is unfavorable in general paresis and tabes, although in the latter all the symptoms may be delayed in their course; no destroyed tissue is ever renewed. In cerebrospinal syphilis complete recovery may at times take place.

Treatment.—I shall only refer to the new remedy, dioxydiamidoarsenobenzol. As yet, in the parasyphilitic affections, it is probably as ineffective as mercury and iodide of potassium. In primary syphilis, it is certainly very active in its results, in certain manifestations more effective than mercury and iodide of potassium.

Whether it will prove effective in preventing the later involvement of the nervous system can only be learned through further experience in its use.

EPITHELIAL OBSTRUCTORS AND CONDUCTORS.

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If you will step into almost any hospital you will see that the members of the staff are neglecting a very important matter indeed: that of the dressing of wounds in such a way as not to interfere with the development of epithelium. You will be surprised at the way this is overlooked by the young men, who are taking a large view of their cases and neglecting details.

Many years ago, at a meeting of the American Medical Association, the chairman asked me to present something, but I told him I had not had time to prepare a paper. He said, "Say something," and on the back of the program I wrote a paper which was published in almost every medical periodical in the world, and immediately brought peroxide of hydrogen into general use. That was almost the worst thing I have ever done.

The most important obstructor to the growth of epithelium in wounds is peroxide of hydrogen. Today, in most of the hospitals of the country you will find the members of the house staff and the nurses obstructing the development of epithelium by the use of peroxide of hydrogen, because it makes things clean; they have the gross idea of cleanliness that would appeal to your kitchen maid, if you have the luck to have that kind of a maid.

The chief obstructor to the growth of epithelium in North America, in May, 1911, is peroxide of hydrogen. The next thing most commonly used is the next most obstructive and destructive, and that is gauze. Absorbent gauze, or any textile fabric, entangles the newly formed epithelial cells, and when it does not entangle them the drying effect allows these poor little cells to stick to the gauze. When, the next day, the gauze is changed to see how the wound is getting on, you will see how it is getting on—just as the man who looked for a leak in the gasoline barrel with a candle found it.

The third, perhaps, most destructive thing is some ointment. Most of the ointments engage hyaline epithelial cells in such a way as to interfere with their activities, and act as mechanical obstructors. The fourth are so-called protecting covers, which act as collectors of culture media and allow decomposition to go on beneath the cover. If we use a covering of gutta-percha for a large area, the fluids beneath immediately undergo decomposition; so we have there another kind of obstructor which is very common.

If you will stop and think you will remember that these things I have described are precisely what you will see in almost any hospital in North America; they are all being done by somebody. The four things which should distinctly not be done are done very generally. You simply have to

observe it. We are so engaged with the new things of the day, the new problems of the time, that they have taken our thought from the matter of epithelium. We have got to get down to the level of our epithelium before we do the best thing for our patients' wounds.

What will protect this pretty blue epithelium? Why, take the inner skin of the egg, for instance; that is one of the most remarkable conductors of epithelium, and when placed next the wound was believed by some of the older pathologists actually to produce epithelium. They thought that the skin part of the egg carried the "vital principle" which belonged to the hen or rooster, I do not know which; at any rate they thought it carried the vital principle and that it manufactured these broad epithelial cells. This was because a wound covered with a large square of the inner skin of fresh egg would sometimes conduct epithelium over a large area, and so quickly that it seemed as if the egg skin must have manufactured the epithelium.

Now, let us take another substance, sterilized animal membrane—Cargile membrane; that also acts as a wonderful conductor, and when it is used large surfaces will sometimes become covered with epithelium in a few hours. If we employ an animal membrane that is benign, if the area is not too large, it will sometimes be covered with new epithelium in twenty-four hours.

Next, as a conductor, we may speak of silver foil. It has a germicidal effect; perhaps I ought not to say that, but at any rate there is a restraining influence upon the development of bacteria. This is one of the very best epithelial conductors—the common silver foil which we find in art stores. Little sheets of it interspersed with sheets of paper may be put in the oven and sterilized at any time, or you can put the foil in a sterilizer and sterilize it in that way whenever you want to use it.

The oiled silks act very well, if properly sterilized, as conductors of epithelium.

Substances which are entirely impermeable to moisture, like gutta-percha, are conductors in a very limited sense. If the material is cut into very narrow strips and shingled so that the serum may escape, it may be used beneath a gauze dressing; but it is rather dangerous. The fact remains that we must have some medium beneath the absorbent medium to allow of good epithelium conduction.

I want to speak, lastly, of gutta-percha tissue, which stands about on the dividing line of the obstructors and conductors, depending upon the wound and the one using the tissue. It is hard to place these conductors until we have by careful study classified them where they belong; the gutta-percha tissue would require a very careful classification as to whether it is a conductor or an obstructor of epithelium.

This question of epithelium obstructors and conductors is one of the most important questions of the day in surgery, and yet one that is most commonly overlooked.

DISCUSSION.

Dr. Gallant: In 1889 Dr. Bern Gallaudet first directed my attention to the unwisdom of roughly removing a dressing from a granulating surface, and by the use

of a magnifying glass demonstrated that in doing so the newly developed, single layer of epithelium was torn off and found adherent to the dry, scab-like gauze. In a paper on the "Treatment of Granulating Wounds,"[1] read before the Surgical Section of the New York Academy of Medicine, Dr. W. W. Van Arsdale presented a dressing of balsam of Peru, 5 per cent.; castor oil, 95 per cent., which when applied to a suppurating surface would act as a moist dressing. This form of dressing does not dry, does not adhere to the surface, keeps the wound free of pus by its absorptive qualities, keeps down granulations to the level of the skin, facilitates the spread of epithelium, can be removed without damage to the newly grown skin, and acts best when the dressing is changed but once in three or four days. Pus retained under a dry dressing is as active an "obstructor" to healing as any we have to deal with, and, *per contra*, the balsam-oil dressing is equally as efficient a "conductor," as we demonstrated in "A Report on the Use of a Mixture of Castor Oil and Balsam of Peru as a Surgical Dressing,"[2] presenting the results of its use in over 29,000 cases. Epithelium itself is the most potent "conductor" if the conditions are favorable, viz., the surface kept dry, granulations kept down to the skin level, and the renewal of the dressing accomplished without injury to the newly developed outshoot. Two years ago I was asked to see a woman whose clothes had been burned from her body some six weeks before. There were several areas of raw, granulating surface, with bleeding from the edematous granulations. At my suggestion the physician gathered up the pieces of dry, exfoliating epithelium from other parts of her body, and distributed them over the raw surfaces, covering them in with the balsam-oil dressing, which was changed every third day without removing the two layers of gauze adherent to the ulcerated surfaces. In two weeks the woman left the hospital with all the areas covered by epithelium. Epithelium may be removed and kept dry for months, and if it is then moistened in salt solution it will rapidly grow on raw surfaces. Rubber tissue over a wound, as pointed out by Van Arsdale, results in reddened and swollen edges, painful to the touch, and produces a macerated appearance. The granulations are exuberant and edematous, and the term of healing is prolonged. It may, however, be used in some cases if slits are cut in the tissue, though the strips must not overlap, lest the secretions seal them together and cause retention of pus.

Dr. J. Blake White: Twenty-one years ago I went to northern New York to see a case in consultation. The physician whom I met asked if I knew Dr. Robert T. Morris, of New York, and had seen what he said about peroxide of hydrogen. I replied that I did not know Dr. Morris very well, but did not believe that he was accurately quoted in all he was reported to have said of peroxide of hydrogen. I believe it has a distinct value in open cavities, but it should be used with proper judgment, and I refer to the incident because it is a pleasure to hear him express himself as he has today about the use of peroxide of hydrogen. This practically corroborates the estimate I placed on his attitude toward it so many years ago.

Dr. Morris: I would like to know a little more about the castor-oil dressing. I understood Dr. Gallant to say that it is an oil dressing which is placed next to the wound; but, according to all my observations of the oils, they interfere with the progress of growth of epithelium. If that is an exception, I would like to know about it. In regard to his blister graft, I would like to say that that is similar to the putting of egg membrane on a wound. I have an article on that subject in one of my books. Just as soon as one of my books is published something comes up that I regret is not in it. As regards silver foil, one cannot say that the galvanic influence is not a stimulating influence, because we know that scarlet red acts more largely than as a conductor of epithelium; it is more than that: it is an actual stimulant of the development of epithelial cells. On surfaces where epithelium production is at a standstill it is possible that the galvanic current may act as an epithelial stimulant, just as does scarlet red.

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[1] New York Medical Journal, July 29, 1893.

[2] Annals of Surgery, September, 1897.

PANHYSTEROCOLPECTOMY FOR HERNIA VAGINAE.

By A. ERNEST GALLANT, M.D.,

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HERNIAL protrusion of the uterus, bladder, and rectum, either singly or in combination, is a too common condition which has taxed the operative ingenuity of gynecologists. There are but few men of wide experience who do not admit of failure in one or more instances. Even after removal of the uterus there has been a recurrence of the cystocele.

It was for this class of patients, and in order to secure the impossibility of a return, that G. M. Edebohls, after four other operations on the same patient had failed to sustain the bladder within the vagina, on April 27, 1900, removed the whole vaginal mucosa, permanently closing the vagina by columnization, and cured his patient.[1] Subsequently he reported having had 8 successful cases; Waldo had 3 cases, and Boldt 2 cases.[2] Christopher Martin, of Birmingham, in 1899, had independently operated on one case of "intractable prolapse," devising a very similar plan; but he did not record it until two years later.[3]

My own experience has been limited to 2 cases, which were reported to the New York Academy of Medicine on January 26, 1911.[4] The first, one of vesical prolapse some years after complete hysterectomy, was as follows:—

Pancolpectomy for External Cystocele.—On April 29, 1909, the whole mucous lining of the vagina was removed, and four purse-string sutures from above downward inserted, columnizing the vaginal walls and entirely obliterating its cavity down to the hymenial border. The patient was out of bed on the eighth day, and has had complete relief from the annoyance caused by the bulging bladder: the backache and the distress before and during her frequent efforts to urinate.

Panhysterocolpectomy.—As an illustration of a case conforming in all its requirements to the warranting of so radical an operation I may relate, briefly, the history of Mrs. B., 68 years old. Mother of 4 children, youngest now 33 years; menopause occurred at the age of 54, fourteen years ago. Four years ago the womb came down so as to be visible at the vulva, and last April (1910) she had a severe cough which drove it completely outside. There had been pain behind the symphysis and in the left iliac region; sanguinopurulent discharge. The uterus projected between the thighs for three inches, and the cervix was the seat of an excavated ulcer which, it was feared, might be malignant.

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1 Medical Record, Oct. 12, 1901.

2 Post-Graduate, 1905, xx, 1245.

3 British Medical Journal, 1901, ii, 974.

4 American Journal of Surgery, June, 1911.

Operation July 21, 1910. A transverse incision was made just inside the hymenial border posteriorly, and a longitudinal incision from the fourchette to the cervix; blunt dissection to the left, repeated on the right. Circular incision, completely surrounding the hymen, and blunt dissection of the anterior half of the vaginal lining, leaving the flaps attached at the cervix. Bladder freed from the cervix; peritoneum entered through the anterior pouch. The posterior *cul-de-sac* perforated; the broad ligaments clamped and the uterus cut free; the stumps sutured individually, then drawn together and sutured. Three purse-string catgut sutures, one after the other, were inserted, great care being exercised in pushing upward the preceding suture before tying the one next below. A fourth suture was placed just within the external opening, and this when ligated completely closed the vagina. The convalescence was afebrile. The patient was out of bed on the seventh day and has enjoyed excellent health ever since, with freedom from her former symptoms.

In the discussion which followed my paper at the Academy, Dr. Boldt said that "if there was complete prolapse of the uterus and vagina there was only one operation to be done—that just described," and that in the 5 cases which he had operated on no drainage was necessary. This was, in his opinion, "the only operation by which one could guarantee a cure of the condition."

The results in the cases reported (21 in all, including Edebohls, 8; Martin, 1; Waldo, 3; Boldt, 5; W. G. Vincent, 1; T. T. Sweeney, 1; Gallant, 2) have been so uniformly successful, the convalescence so satisfactory, the post-operative effects so slight and free from complications, and the reports from the patients so gratifying, that it seems to us justifiable to recommend this operation in severe forms of prolapsus, especially where other operations have failed, provided (*a*) the woman is incapable of impregnation or past the child-bearing period and the menopause, and (*b*) that the husband is willing to forego marital relations, or (*c*) that the patient is a widow who believes that she can forever abstain.

DIABETES MELLITUS FROM A SURGICAL STANDPOINT.

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For many years it has been customary to examine the urine of all surgical patients, at least for chemical reaction, specific gravity, albumin, and sugar. These tests may show nothing abnormal, or they may lead to extensive chemical, microscopical, or bacteriological examinations. They should, therefore, be accurate and positive. Though they are few in number and simple in character, mistakes have been made. Mistakes have been made by inferring no sugar from a low specific gravity. Mistakes have been made by not knowing that albumin will interfere with the copper test for sugar, and that if present it should be separated by boiling and filtering the urine before using this test. Mistakes have been made by inferring the presence of sugar on using old solutions, or from late reactions due to the presence of uric acid or other reducing substances. When the action of the copper solutions is doubtful, the yeast test, collecting any carbonic acid formed, should be used; but this is rarely necessary.

As the finding of albumin leads to a microscopical examination for pus, blood, or casts, so the finding of sugar should always be followed by further chemical examinations to determine the presence or absence of other substances of still greater significance. It is of great importance to examine for the acetone bodies: acetone, diacetic acid, and betaoxybutyric acid. These appear in the urine in the order named, and disappear inversely. If there is diacetic acid, there is usually acetone. If there is much diacetic acid, there is usually betaoxybutyric acid. As the test for the diacetic acid is simplest, it is used first. It is made by adding a few drops of a dilute solution of perchloride of iron to the diabetic urine. If diacetic acid be present, the color changes to a garnet, varying to almost black, depending on the amount of the acid. The tests for acetone and betaoxybutyric acid are not difficult, and need not be described here. If the acetone bodies are found, it is then of great importance to examine and determine any increase of the carbonate of ammonia.

The presence of glucose and acetone bodies, and of an increased amount of carbonate of ammonia, is very significant. The glucose signifies a disturbed metabolism of carbohydrates and not infrequently of the animal starch, glycogen. The acetone bodies signify a disturbance of the metabolism of proteids and fats, especially the latter. The increase of the carbonate of ammonia signifies a disturbance of the proteids. The disturbed metabolism of the carbohydrates, fats, and proteids in foods ingested, or in the formed tissues of the body, necessarily has to do with the nutrition, repair, heat, and energy of the organism, and, of course, merits the careful consideration of

the surgeon in diabetic cases. The evidence of disturbed metabolism is made positive by the examination of the urine, but its full significance can be ascertained only by a careful consideration of the foods taken and a general examination of the body. All the abnormal conditions found in the urine of diabetes may be produced artificially by foods alone. There is no other disease where improper diet is so generally advised and used, and is so injurious, as in diabetes. It is, therefore, especially important that the surgeon find out what foods a diabetic has been and is taking. It seems sometimes that the finding of glucose in the urine gives rise to a condition which might well be called "glycophobia" in both physician and patient. Both seem seized with the insane desire to remove every particle of sugar and starch from the diet. No well person could stand such a sudden change of diet or such an unbalanced nutrient ratio without suffering serious impairment of health. Nor is it surprising that the diabetic under such treatment fails rapidly in flesh, strength, and health, which are of such vital importance in resisting the disease. The injurious effects of such a course of treatment are manifested in the urine by the increase of acetone bodies and carbonate of ammonia, compared with which glucose is of little importance.

It might be fairly asked, "If the blood contains an excess of glucose, one of the end-products of carbohydrate digestion, why cannot this class of foods be omitted?" This question should not be asked of the reasoning faculties, but of the body. The body says, "Glucose adds fuel to the fire in diabetes." The body says, "Sugars fermentable by yeast into glucose do the same thing." It is a case where one man's food is another man's poison. The body says, "The removal of all carbohydrates from the diet gives rise to most serious metabolic changes." The body says, "Starch in some form is necessary to life even in diabetics." The body says, "Starch requires and promotes the activity of the salivary glands, the pancreas, and intestinal glands, and sets in action the whole machinery of digestion, which is so necessary to health." The body answers the question, then, by advising no glucose, no fermentable sugar, but at least three ounces of starch daily to each 150 pounds of body weight. The body says that the reduction of the glucose in the urine may require some reduction in the quantity of proteid foods, and that for the reduction of the acetone bodies there may be needed an increase of starch or a reduction in the fat foods, especially in those containing the lower acids, as butter, cream, etc.

The best test of the value of foods is the maintenance of the body weight, strength, and energy. These should be carefully noted by the surgeon and solicitously maintained, even at the expense of a little sugar in the urine. Should, however, the patient be losing flesh, the surgeon should note whether it is adipose, or muscular, or both tissues which are being consumed. If the loss includes the muscular tissues, then the same substances are affected that are most needed in the repair of tissues.

It should also be borne in mind that the loss of flesh, strength, and health in diabetics may be due to some complication, as tuberculosis, to which these patients seem especially liable. When a diabetic is losing or is in

reduced health and flesh, in spite of sufficient food, and is carrying a slightly varying temperature, we should be very suspicious of tuberculous disease. This complication should be taken into account before advising certain operations.

The examination of the blood of diabetics is necessary and of importance to the surgeon. The condition known as lipemia—an enormous increase of the minute fat globules in the blood—may exist. This is easily recognized by the osmic acid stain, by the separation of a few drops of blood into an upper white and lower red layer, or by the milky appearance which occurs when the blood is shaken up with chloride and citrate of sodium solution. This condition is not very common, but, as the running together of the oil particles on interference with the circulation may produce thrombi as complications, or emboli of the brain, heart, lungs, etc., serious disturbances may ensue, especially after operations.

The examination of the blood may also help to determine the resisting power of the patient to infection from streptococci and staphylococci. My study of this subject in diabetics shows that many diabetics have a normal resisting power, and operative experience confirms it. It is also true that in many there is a lowered resistance, as is likewise confirmed by experience. We should not, therefore, draw general conclusions from either class of cases, but consider each case by itself.

The existence of irritating substances in the blood of diabetics gives rise to endarteritis and arteriosclerosis, and, consequently, to sclerotic and degenerative changes in the various organs and tissues. These vascular changes should be observed and carefully examined by the surgeon, as they give rise to impaired nutrition, interference with the healing processes, and lowered tissue resistance to infection. While gangrene in diabetics may be of the infectious variety, it is generally due to the arteriosclerosis, which obliterates the vessels by thickening their walls or promoting the formation of thrombi. These results are found in connection with the smaller vessels and those farthest from the heart. The surgeon must watch carefully and endeavor to promote the circulation, especially in the lower extremities, and study the condition of the arteries in determining the location for the operation and in making his flaps.

The lowered resistance of some diabetics may be still further noticed in the presence of boils, carbuncles, and infections following slight injuries. A careful examination of the skin and mucous membranes may, therefore, help in determining the state of health. The history of the repair of slight injuries should also be taken into account before surgical operations.

It is very evident that diabetics present various types and conditions, and that the term diabetes mellitus conveys no definite concept or group of symptoms to the surgeon or physician. When it is said that diabetes contraindicates certain operations, some more definite reason should be given. Diabetics present a number of different types or groups besides acute, subacute, and chronic, or mild and severe cases. It is well for the surgeon to classify them, even though dietetic or other treatment may change them from

one class to another. These cases should be considered in the class to which they belong at the time of the operation. They may be divided into two general classes, one containing those having glucose only in the urine, the other containing those having glucose and the acetone bodies in the urine.

The first class may be subdivided into two classes, one in which the glucose comes from carbohydrate foods taken, the other in which sugar persists when carbohydrate and proteid foods are restricted. The first class of cases varies very much as to the amount of carbohydrate foods that can be taken without glycosuria. Sometimes the omission from the diet of sugars alone is sufficient to remove the glycosuria. Sometimes a slight limitation of the starch, as well, will produce the same result. Dietetic and other treatment for a time may produce a still further tolerance for starch. This class of cases, and it includes many, offers little if any contraindication to any operation. Cases of the second class under dietetic and other treatment may have but a small amount of glucose in their urine, and generally become unconscious of any impairment of health. These cases bear operations well, with careful attention.

The other general division, embracing those cases with both glucose and acetone bodies in their urine, may be subdivided into three classes. The first one includes those in which the acetone bodies are due to improper diet. The starch taken is insufficient. As a result of increasing the starch the acetone bodies disappear from the urine, and these patients must then be considered as belonging to the other class of diabetics. The injury done by the improper diet is relieved in a short time. These cases also, after a brief treatment, show but little disturbance under operative procedures.

The second class of these cases includes those in which the glucose and acetone bodies are due not only to foods taken, but to changes in the body-tissues themselves. These cases are of a more serious character. Changes in the adipose tissue are of less serious import than those in the muscular tissue, as has already been mentioned. In these cases the general condition of the patient, the nature and need of the operation, and the amount of carbonate of ammonia in the urine should be taken into account in deciding upon an operation.

The third class of these cases is a severe form of the second class, and shows urine containing glucose, acetone bodies, and a marked excess of carbonate of ammonia. They are the most serious cases; yet much can be done to put them into the other classes and, if possible, this should be accomplished before operating.

The condition of the kidneys should not be lost sight of in this connection. Two forms of nephritis may exist in diabetics, the parenchymatous form, due to the excessive activity of the kidneys and the irritating substances eliminated, and the chronic interstitial form, due to the endarteritis and arteriosclerosis.

The knee-jerk should be tested, as its absence indicates impaired functional activity or sclerotic changes in the central nervous system.

A word might be said in regard to heredity in diabetes. Heredity may

give rise to a lowered resistance to the disease. We have to consider the influence of heredity on those who do not have diabetes and on those who have, so far as operations are concerned. As for those coming of diabetic families, but not suffering from the disease or the nutritive disturbances incident thereto, the matter of heredity requires but little attention. As for those having diabetes, they should be considered just as others of the class in which they belong. They are generally mild cases.

The matter of preparing a diabetic for an operation is certainly worthy of careful consideration. The circumstances of the case, as in accidents and emergencies, may allow of no preparations except those directly connected with the operation itself. Fortunately, such instances are rare. When there is time for preparation the most serious mistake made is to put the patient on a carbohydrate-free diet for a few days, with the idea of getting the excessive amount of glucose out of the blood. Those who do this do not study any other changes in the urine, and do not realize that by this course mild cases are made worse and severe cases are made much worse, and may even be brought into a state of coma with fatal termination. The best method is to put the patient to bed for a few days. Rest lessens food requirements and the activity of tissue change. Water should be freely supplied to dilute the poisons in the blood and promote their elimination. In the way of food, starch, to the amount of three ounces in twenty-four hours for each 150 pounds of body-weight, should be allowed. White bread, potato, oatmeal, or rice may be used. Sometimes one food acts much better than the others, but it is generally better to use a variety at this time. The amount of each will depend upon its percentage of starch. Thus, white bread contains 50 per cent. starch, potato 20 per cent., oatmeal 70 per cent., rice 40 per cent. For proteids, beefsteak, chicken, and eggs may be used. For fats, the fat of beef, oleomargarine, and olive oil do very well. Celery, radishes, lettuce, and cabbage form good green stuffs. For drinks, water, tea and coffee without sugar, brandy, whisky, and fermented wines may be used. As a tonic, strychnine sulphate, gr. $\frac{1}{30}$ every four hours, can be given. When there is edema some form of iron is advisable. Thirty grains of bicarbonate of soda every four hours is helpful, but if there is much acidosis it should be given every two hours. When the acidosis is severe it is better to omit butter and cream. As laxatives, rhubarb and soda, cascara, castor oil, and mercurials are useful. Water alone, freely taken for twelve hours before the operation, favors elimination, and is accompanied by no ill, but rather exerts a beneficial effect from lessened metabolism. Care should be taken that the minimum amount of starch required be added to the diet as soon as possible after the operation.

The choice of an anesthetic, as well as its administrator, is of importance. Chloroform sometimes causes acetonuria in health, and should not be used. Nitrous oxide, even with oxygen, may be associated with cyanosis, and should be avoided. Ether also may cause acetonuria, but is safest and best. The etherizer should be one whose presence inspires confidence, obedience, and hearty co-operation, and whose experience tends to the use of a small quantity of ether, free admixture of air, freedom from cyanosis and other annoy-

ing disturbances, and to the relief of the operator from some care, annoyance, and loss of time.

There is no operative treatment for the cure of diabetes, but the disease is benefited by whatever improves the general health. Operations are for complications and for whatever surgical diseases or conditions may arise.

The boil in diabetics is not uncommon. Cleanliness by frequent bathing and freedom from rough clothing, collars, and cuffs are of great preventive value. When taken early, boils may often be aborted by rubbing in a 2 per cent. ointment of the yellow oxide of mercury and hydrous wool-fat. If they persist, tonics, vaccine, antiseptics, free drainage, and sometimes excision of the diseased tissue are valuable. The bathing of the parts several times daily with an antiseptic solution for two weeks after the parts are healed may prevent further infection of the area involved.

Carbuncles require similar treatment, but when the tissues show but slight resistance early and thorough removal gives the best results.

Balanitis with phimosis should be treated by taking out a V-shaped piece of the dorsal part, as this acts like a short incision and facilitates healing. A few stitches should connect the upper and lower surfaces. Cocaine is a sufficient anesthetic for this procedure.

Gangrene often calls for surgical treatment in diabetes. While the various forms of gangrene may occur, it is here generally due to arteriosclerosis. The treatment is preventive, palliative, and operative. We have watched with dread and a sense of helplessness the gradual failure of the circulation, the formation of thrombi, and the approaching death of the part; but now a ray of light comes from the suggestion that a new access of blood may be provided by anastomosing the femoral artery and vein. This operation should be done before the gangrene appears. The results of such operations will be awaited with interest. As slight injuries may start the gangrenous process, such injuries, even the trimming of corns, should be avoided. The local palliative treatment consists of the use of antiseptics and the drying of the dead part by means of hot air.

In cases of gangrene of a lower extremity the disease may affect but one or more toes. In these cases if the line of demarcation forms early, if the adjacent parts are not inflamed, and if there is a good pulse of the posterior tibial artery behind the internal malleolus and of the dorsalis pedis artery, the removal of the dead portion alone may be sufficient. If, however, the line of demarcation forms slowly, the foot is inflamed, and the pulse of the posterior tibial and dorsalis pedis arteries is but feebly, if at all, felt, operations on the foot are harmful. In these cases the amputation should be done above the knee.

In these amputations of the thigh the Esmarch bandage, the tourniquet, or constant pressure on the upper femoral should not be used. To stop the circulation even for a short time, in a part suffering from lack of nutrition, and to leave such tissues in contact with those affected with gangrene, promotes gangrene and infection, and is a serious mistake. To operate without arresting the circulation is easy. When the parts are prepared a circular

flap of skin and connective tissue is made and turned up. The small vessels and large veins are clamped. The muscles on the back and sides of the thigh are then severed, and the vessels here also are clamped. The periosteum is then divided and peeled up, and the bone sawed off. The large femoral vessels are then clamped, and the remaining tissues severed. This method of amputating the thigh while a good circulation is being kept up was called to my attention a number of years ago by Professor Kocher, of Berne, and I have since used it with great satisfaction. If, on severing the large vessels, they are found to contain clots, these may, one at a time, be loosened by a probe and expelled by the force of the blood-pressure, an assistant seizing the femoral as soon as the clot is expelled. This procedure promotes circulation, may save a second amputation higher up, and provides a healthier stump.

The diabetic may require any form of surgical procedure. Because of his disturbed metabolism, his impaired nutritive and reparative processes, his reduced resistance to infection, and his depressed nervous system, he requires the most careful consideration of the surgeon and the most skillful application of the principles of surgery in the treatment of wounds. There should be the most careful cleanliness and antisepsis, free drainage, the least possible injury of tissues, the best circulation for flaps, careful apposition of parts to facilitate healing, incisions as small as are consistent with dexterity, suturing with proper tension, and careful protection of the parts. If these precautions are properly observed, and the patient is properly prepared for the operation, a large proportion of diabetics can be operated on as safely and satisfactorily as any other class of individuals.

In this brief paper on diabetes mellitus from a surgical standpoint, I have tried to emphasize the importance of a careful and complete examination of the urine and a study of its changes, a consideration of the metabolic changes taking place in the foods and tissues of the body, especially as regards nutrition and the processes of repair, and the need of a general examination, including the blood, blood-vessels, skin, kidneys, and resisting power. I have tried to classify cases of diabetes and to suggest how to prepare them for an operation. I have emphasized the importance of ether, of an experienced anesthetist, and the most skillful application of surgical principles.

There was a time when surgery was defined as that part of the healing art which requires manual or instrumental means in the treatment and cure of disease. There never was a time and never will be a time when the surgeon will be a mere tool, for he is brought to the consideration of those processes and diseases which call for the finest training of the mind, the most complicated study, the most conscientious, strenuous, and heroic efforts. In short, he should possess all these qualifications, which, combined, make him the noblest helper of his fellow-man.

DISCUSSION.

Dr. Sajous: I wish to say that I agree perfectly with what Dr. King said on the medical side of the question. There is absolutely no doubt that the treatment that has been followed has been more deleterious to patients than otherwise. Eight years ago, if Dr. King will kindly look at my work on the "Internal Secretions," he will

find the same ideas that he has advanced, *i.e.*, condemnation of the absolute elimination of carbohydrates from the diet of diabetics. The moment we eliminate carbohydrates from these patients' diet in fact, that moment they begin to fail, or, as Dr. King once put it, they begin to die. I have called attention also to the fact that we should recognize two classes of cases: the sthenic and the asthenic. In the former excessive carbohydrate catabolism prevails, and any agent which enhances this—strychnine, for example—is harmful. Such patients are usually irritable and may appear plethoric. In the asthenic cases, the opposite condition is present; general metabolism is slowed, and the prevailing state is virtually one of alimentary glycosuria. Such patients require the opposite treatment, *i.e.*, one calculated to enhance metabolism,—tonics, etc. In one of my cases, the results were so admirable that the patient, a physician, exceeded my instructions, and so actively took strychnine, phosphorus, digitalin, and other agents that he brought on various manifestations of intoxication. Properly differentiated, however, and their treatment judiciously regulated, these cases do far better with carbohydrates, especially potatoes, than without them.

REMARKS ON THE TREATMENT OF CHRONIC DISEASE.

With Special Reference to Simple, Efficacious Remedial Measures Readily Applied, but Often Neglected.

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"There is nothing which so conduces to length of years as an incurable malady."—*Oliver Wendell Holmes.*

MANY effective methods are known for relieving and curing chronic disorders. Some are better than others, but the best are no better than the worst unless pursued with consistency, persistency, and, above all, appreciation of the physiologic factors involved.

All remedies for diseases are valuable in proportion as they render available inherent self-protective and self-reparative powers. The body, moreover, is a concrete, living entity, not made up of separate parts, like an insentient machine, any one of which is capable of acting and reacting independently of the rest. In the sentient human machine, wherever there is local damage or derangement this can be removed only by eliciting the full co-operation of all the component mechanisms, and being aware of the interdependence of every part. Nowhere is the significance of this co-operation of all parts more direct and important than in the treatment of protracted disabilities, and for many reasons. Among these is that, whereas in traumata—fractures, wounds, and other strictly localized damagements—the remainder of the organism is presumably at the time in a state of full integrity (hence, with full capacity for prompt and complete repair), conditions are quite otherwise in protracted, long-prevailing disorders, the results are manifest in slow, but steady disintegration of tissues,—in the retroaction caused by depression in both the psychic and physical spheres of activity. Unless the individual is regarded as an all-round well-balanced organism, with full consideration of all the essential factors constituting health (not forgetting permissible variants), the best results cannot be attained, either in conservation or repair.

In acute disease, notably the infections, there is fever, a defensive process whereby the autoprotective forces are aroused to the performance of their most perfect work. Much can be done to control and direct them. The problem is then relatively simple, since the organism is presumably normal when infected.

In chronic disease, the defensive powers are gradually overwhelmed, the vital forces exhausted in varying directions and degrees. No longer can they be relied on promptly and efficiently to meet and overcome morbific agencies. Not only so, but the causal factors become increasingly complex,—a blend of psychic confusion, loss of physiologic conservation, and structural disintegration. Be the factors few or multiple, the whole symptom-complex becomes one

of impairment not only of the governing vital mechanisms, but of the entire organism. Therapeutic agencies must, then, include systematic encouragement of all functions, rehabilitation not only of disordered noble organs, but of systems deranged as a whole.

Hence, the best remedies consist in conserving the action of circulation, respiration, metabolism, etc., not forgetting the inevitably impaired consciousness. Mental deviations invariably occur in all protracted disorders and must not only be first considered, but in all stages reckoned with.

The circulation stands next in importance, and the fact that the skin area is the largest, most readily influenced factor in sensation and reflex irritation should never be lost sight of.

Respiration stands at the basis of oxygenation, but the muscular system is an efficient ally. Both require education and exercise. The digestive organs, elaborate as they are, cannot carry out their complicated program unless they are, and remain, in full accord with the entire group of hydrostatic mechanisms. They cannot act and react harmoniously unless they be, and remain, in normal, or nearly normal, mechanical interrelationships one with another, their centers, nerves, and connecting parts unimpaired by faulty position, torsion, compression, or by disarranged or inadequate support from relaxed or feeble external walls. The integrity of the skeletal structures here exercises a powerful contributory influence. Not only must these gross structures be maintained at their best, but wherever they suffer impairment beyond a certain degree the integrity of the vital processes suffers to an extent too generally overlooked. Elasticity is an essential factor in all tissues, except a few, like the bones, ligaments, and tendons. Hence, loss of tissue-tone, rigidities, adhesions, excessive compressions, and relaxations are factors which demand full consideration in solving any problem of long-standing functional disrepair.

Chronic morbid processes, while of wide diversity and due often to special disease entities, nonetheless are at bottom mere outgrowths of vitiated physiologic processes. Physiologic processes are uniform in their manifestations not only when normal, but also when deranged. The human organism is disturbed by disease, of whatsoever nature, along strictly analogous lines. The special features may and do vary, but chiefly in accordance with the structures altered, rather than by reason of the nature of character of the disease itself. The essential machinery, the vital processes of life, growth, change, and repair, can, if rightly conserved, be made to do its work as well as the damagements present permit. Hence, the organism as a whole is usually capable of recovering a fair measure of efficiency. Thus, it is the duty of clinicians so to enhance the autoprotective and regulative mechanisms as to compensate for the specific damagements.

This truism may seem so obvious as to need no elaboration, yet clinicians too often overlook the fact that these deranged physiologic processes can frequently be so utilized and enhanced as to secure degrees and kinds of betterment not always otherwise obtained.

In brief, I maintain that there is urgent need of a well-rounded presentation of the clinical pathology of chronic processes. So far as I can learn this

does not exist. We want systematic generalizations on morbid physiology of protracted disorders. This will prove of practical aid for clinicians in determining the character, scope, and remediableness of widespread losses in organic integrity.

Often closely analogous phenomena arise in persons suffering from morbid states widely divergent in essential pathology. Our remedial resources in chronic disease depend for efficiency upon a correct appreciation of: 1, the particular disease process; 2, what remains of the reparative powers of the individual as a whole; and 3, the degree and quality of the integrity of the structures deranged, damaged, or destroyed.

Among our medicinal agents there are a few, very few, drugs which are called *specifics*. These fluctuate in our confidence, at times fail, and occasionally (as in the case of the loudly heralded Ehrlich remedy) open the door of hope. The utmost they can accomplish in chronic disease is to unlock the avenues of toxic wastes, to overcome the specific agency so far as it continues to be forceful, and to free the organism of the immediate disabilities thereby caused. At best their limitations are most narrow.

Always behind the toxic entity there is a damaged human organism, a suffering animal, whose recovery depends in the final issue upon how far it is possible to reawaken and redirect the inherent forces which sustain and maintain life.

Here is a field of opportunity, of scientific research, which, in my judgment, is not adequately explored; certainly not presented to the student as hopefully and systematically as the facts warrant.

Empiricism in these days of scientific advance is decried, yet the best results are often obtained by those who are equipped rather with good common sense, fortified by a practical knowledge of the physiologic resources of the organism. Too often the ultrascientific physician belittles this phase of clinicism and his unrelieved patients wander to strange apostles of health and get well.

Every one of us has experienced this chagrin. Now how do these extramural healers, these loud-boasting pretenders, manage to make good.

Plainly, they appreciate, apply skillfully and confidently, well-attested empirical remedies directly along the line of obvious needs for the individual. It has been by custom whenever an unrelieved patient has left me and obtained satisfactory results at the hands of some irregular healer to do my best to find out what was done and how. My experiences would form material for an interesting paper. In every instance I learned something worth knowing. Sometimes it was a new idea, a useful generalization, or a novel phase of well-known principles.[1]

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[1] Having for thirty years had a keen desire to improve my therapeutic resources, I have preserved clippings from medical and other literature containing hints which appeared useful. On reviewing these it is remarkable how many invaluable suggestions are to be found, insufficiently emphasized or made clear, yet taken together, capable of adding much to our all too meager means of restoring lost vigor.

From a wide reading on those subjects which constitute non-pharmaceutic therapeutics, it seems to me of use to present personal convictions deduced from experience to illustrate my contentions.

Clinicians do not seem fully to appreciate one fundamental principle in all therapeutics, viz.: the scope and efficiency of scientific personal hygiene and its special applicability in the treatment of chronic disease states. In my lectures I group the subject under three heads:—

1. *Conservative Personal Hygiene.*—Including those well-recognized and commonly observed rules of conduct which are supposed to be known and accepted of all physicians.

2. *Constructive Personal Hygiene.*—The selection and application of the best determinable means of so regulating human conduct as to raise the kinetic index to the highest dynamic possibilities, so that a practical equilibrium shall be attained. A large subject this, the basis of which lies in taking a broad view of physiologic laws, the utilization and enforcement of which will go far toward raising any individual (of average vital integrity) to a higher plane of efficiency. Every individual possesses vast unelaborated or unappreciated potentialities never hitherto utilized, and which it is the duty of the physician to estimate, and to teach how they shall be made available.

3. *Reconstructive Personal Hygiene.*—The subject of the present communication. Reconstructive personal hygiene may include all those agencies and procedures whereby an organism below the norm of efficiency, deranged or chronically diseased, can be raised to a higher plane, of original efficiency, or restored from damagement or long-standing disease. The dynamic index resides in the regulation of conduct. The coefficient of efficiency in each one is seldom known.

Personal hygiene may be defined as the scientific conservation and amplification of the body forces to secure potential equilibrium. The current conception is rather the practice of well-known rational measures for maintaining health. There is ample evidence to warrant the assumption that constructive personal hygiene is itself a science, and fully deserves to be developed as the most promising agency in both prevention and cure of disease. Adequately elaborated, it is capable of rendering increasing and almost limitless service to scientific medicine. Alone it can never suffice. Its powers can readily be overestimated—they often are.[2]

Two thoughts at once obtrude: 1. Our conception of the physiologic action of drugs demands critical and thorough rebuilding. This Sajous has done. 2. The whole subject of scientific hygiene demands equal attention with pharmacotherapy.

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[2] For example, there has been within a decade a notable evolution in the treatment of tuberculosis. I have heard a professor of clinical medicine assert, in a popular address, that the whole treatment of this infection now consists in fresh air and plenty of food, drugs being useless. Similar statements are constantly appearing. If they were true, then would the labor and self-sacrifice of the ages be rejected not only by the votaries of science, but by the laity, who are all too ready to belittle our careful observations and exact findings. Therapeutic nihilism is both false and hurtful to the best interests of the race. Nonetheless, the revolution thus indicated is significant.

It is a significant fact which the medical mind is inclined to ignore that many valuable systems of healing originate among, or are brought to fruition by, overenthusiastic irregulars, whence they are forced on our attention. It is wise to accept the hints furnished, make researches into the essential principles involved, and to acquire skill with those remedial measures demonstrated to be sound. Some are invaluable, as I shall show. By means of them results can be obtained in certain disorders greater than by others now in use. At the worst, they afford convenient, efficient accessory and reinforcing curative agencies. We should realize the value of extramural healing methods, pick the meat out, and give our patients the benefit of whatever in them is worth while. There can be no doubt of brilliant cures effected by enthusiastic ignoramuses, or earnest men of one idea.

No alert business man or manufacturer would lose a chance to better his methods. Yet, medical men exhibit a stolidity, an indifference to flagrant inroads upon their domain, with a fatalistic philosophy or peevish denial of plain facts. Some of the cures wrought by irregular empirics are only partial, relief being obtained for the more obvious distresses; the ultimate lesions persist. It is our business as apostles of science to afford equal or better relief. The day of specific medication is past, despite occasional bursts of brilliant meteors like salvarsan or vaccine therapy. Recovery from chronic ailments will be achieved most largely by conservation of natural powers. Here, again, we find the burden of evidence in favor of the efficiency of rational agencies, included under the term *reconstructive personal hygiene.*

In almost every individual afflicted with protracted disease the latter is complicated by disorderliness in the mental and emotional spheres. Unless these aberrancies are reckoned with, the springs of thought and action, and especially feeling, set in order, balanced, rendered more normal and systematic, a large part of the symptom-complex persists. The feelings, disordered as they are, need full consideration, skilled interpretation, and sympathetic direction. The mind may be clear and efficient in some respects, but in others is not, and should be put into splints, rested, soothed, and restrained.

Especially are responses to physical stimuli from within liable to be misinterpreted, the more important ones subordinated, and the lesser ones exaggerated. Some lesions of gravity are wholly non-sensory; at least, awareness has not yet arisen to the threshold of consciousness (*e.g.*, abscessed teeth, impactions, splanchnoptoses, and other latent lesions capable of exciting complex distresses). Disturbances thus established between receptivity and determination have, then, become more or less automatic. They exert a persistent effect on physiologic integration, aggravating any existing minor departures from the norm. It may well be, as Charles L. Dana asserts, that there are no functional neuroses or psychoses. Disorders so initiated vary in proportion to the progressiveness of the functional eccentricities and the susceptibility of the consciousness, its propensity to go astray, or aptness to dominate the physiologic processes; in short, complex diseased states depend for solution upon the subserviency of the body to the directing agencies, conscious or intuitive.

A reasonable familiarity with neurology and psychiatry would, then, seem to be a prerequisite in rightly handling chronic disorders.

Even as drugs in small or large doses exert different effects, both in kind and degree, so are physical or hygienic measures followed by good or ill in proportion to judicious, systematic, or to indifferent direction and employment. Moreover, any remedy may at times act in a manner, or on a function, not expected or foreseen, for good or for harm, and this is often realized only by close observation (*e.g.*, thyroid extract in insomnia due to vague gouty symptoms—saline enemata in rheumatoid arthritis—removal of abscessed teeth in serious psychoses, etc.).

The whole problem of nutrition is shown by Horace Fletcher and others to rest largely on how food is prepared, selected, and, above all, masticated. High and low proteid dietaries, intestinal putrefaction, and the like questions settle themselves often by self-regulation of tastes or growing awareness of instinctive needs, learned through revised habits of eating.

So skin hygiene, consistently utilized, is capable of more than conservation, even of radical reconstruction. Facts brought accidentally to my attention have led me to secure unexpected and gratifying results by this means in manifold incurable states, as in chronic nephritis, gout, myositis, so-called chronic or muscular rheumatism, disintegration of circulatory structures and of the central nervous system. A diseased kidney is often normal in parts, and to its ability to regenerate there is no known limit.

The principle of action, briefly, is to insist upon skin friction, prolonged and thorough, daily or oftener, by the patient or another, with or without heat and cold, salt, or oily inunctions, or other adjuvants.[3]

In this connection it may be remarked that habits of home bathing, even among the most intelligent, will often be found on scrutiny absurd or worse. Judicious regulation of home hydrotherapy can, and often does, secure gratifying and permanent effects on circulatory balance, notably the neutral immersion bath in arteriosclerosis, cerebral excitement, insomnia, and a wide group of hitherto-unrelieved disorganizations.[4]

Water externally is only second in importance to water internally. The history of spa treatment furnishes massive evidence worth studying. Colonic irrigation not only cleans out the lower bowel (made classic as a danger

[3] The treatment in one "fake cure" consisted of persistent skin friction applied over the entire body with a piece of haircloth moistened in a solution which I had analyzed and found to contain ammonium chloride. Ferrier (British Medical Journal, April 16, 1906) calls attention to the tabetic ataxy being due to impoverishment or loss of centripetal impressions of all kinds, conscious as well as unconscious; a default of the centripetal and subconscious impressions. Hence, this skin stimulation doubtless produces good effects in some cases, as I have found by experience. The one measure most emphasized by the proprietors of a certain kidney belt is skin friction to a degree of thoroughness most interesting. I have the privilege of knowing the principal, a man of wisdom and charm. He secures remarkable results by himself training the patient in reconstructive hygiene, insisting on daily skin friction of from one to two hours.

[4] To relieve high vascular tension and the varied group of discomforts and dangers which follow, nothing is more efficacious than a neutral immersion bath, of 100° F., for from half an hour to two hours.

center by Metchnikoff), but also furnishes the best and simplest relief from toxic effects in many forms of genitourinary disorder. This diuretic action of colon-flushings—really invaluable—is alluded to in literature only incidentally, though it furnishes an excellent remedy in many chronic disorders where the heart and kidneys are competent and renal inadequacy is a feature. Of course, one should be careful to avoid overmuch of fluids in chronic nephritis and high blood-pressure with a weak heart.[5]

Respiration, commonly regarded merely as an automatic function, is capable of education and development into a potent agency for conservation and reconstruction, as the Yogis of India, and endemic enthusiasts elsewhere, have abundantly demonstrated—even after their claims are heavily discounted. My own experience with systematic respiratory education has been gratifying, especially in strengthening bed-ridden, lame, or otherwise handicapped folk. The use of this measure in chronic cardiac disease is plainly desirable.

This brings us anatomically to another auxiliary agency, which has apparently been left for me to emphasize, viz., increased elasticity of the skeletal, ligamentous, and other mobile structures as a factor in sustaining vigor.[6] To secure results from respiration obviously the thoracic structures must be normally elastic (they seldom are in middle-aged persons), and also the abdominal muscles must preserve normal tone—they very rarely do. Here educational exercises are required and accomplish much.

Note one practical need for mobility which at first presentation may cause demur, though experience emphasizes its truth: In the spinal column originate and are contained thirty-one pairs of spinal nerves. Between each two vertebræ lie cell-bodies closely concerned, among other duties, with vasomotor innervation. I have elsewhere elaborated this subject (as well as many other of the foregoing hints) and here can only offer conclusions. It is of deep significance to the welfare of symmetrical vasomotor action that the erector spinæ muscles, innervated as they are by the posterior primary divisions of the cord, shall be, and remain, normal and elastic. Correct posture is a corollary of elasticity. This includes the whole subject of mutual interrelationships of the viscera.[7] Attitude bears a close clinical relationship to normal functionation: *e.g.*, defecation, parturition, etc.

Coincidently with this subject is to be mentioned the exceeding importance of scientific manipulations, nerve-pressures, which form the basis of the successful, but overstated claims of certain *extramural* cults designated by picturesque, pseudoscientific names. Accident drew my attention to this subject thirty years ago, and since then I have placed on record my experience and convictions. Time and fuller experience confirm me in my earlier views. I am now prepared to urge the use of dexterous hand treatment—light, skillful

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[5] Colonic irrigations, employed in over a dozen bad cases, afforded a surgical friend of mine a curious and undesired reputation as a specialist in rheumatoid arthritis.

[6] The late Sir Herman Weber, of London, in a personal letter asserted as his opinion that I had pointed out in a paper (Popular Science Monthly, March, April, and May, 1904) the most potent factor in the aging of tissues—loss of elasticity—and in its conservation, the best means of securing longevity.

[7] See paper, Journal of Advanced Therapeutics, March, 1911.

nerve-pressures, done by, or strictly supervised by, the physician—as one of the most potent agencies in both diagnosis and treatment. By it can be achieved the cure or relief of many morbid states possible in no other way known to me. Physicians in the near future will realize the truth of this assertion. Hitherto the methods advocated, while at times efficient, have been of the crudest: *e.g.*, unskilled massage, bonesetting, etc.

The effects produced by skillful finger-pressures on the erector spinæ muscles are very patent and prompt. Blood-pressure can be raised or lowered. The effects are most marked where tension is abnormally high, and the relaxation of the peripheral vessels is so pronounced as not seldom to induce free sweating. This does not go further—never below normal for the individual. The best results are seen in high tension due to disease of the heart muscle. A young friend of mine, Fred Erdman, has devoted much study to the effects of manipulation; his observations are exact and growing numerous. He tells me he has reduced pressures from an excessive tension as much as 50 mm. Hg.; more commonly, 30 or 20 mm. Hg. My own observations are analogous, though less numerous. Low tension below the norm can also be somewhat raised; the effects, however, are not so lasting. My own experience leads me to assume that here we have an agency for the regulation of vascular tension which will prove safe and efficient.

As a means of distributing blood, and hence restoring deranged function, these nerve-pressures afford a large field of usefulness. Thus, in long-standing derangements of the digestive tract I have often been able to get permanent betterments; not only where surgical measures had been decided upon, but after operation had furnished no relief, function was restored by their use.

Surface structures in chronic states frequently need support, mild compression, agencies which call and keep the blood to a locality. This relieves sensory disturbances, even when deep-seated, invites phagocytes, and in other well-known ways encourages dormant activities. Bier's methods are valuable, but at best they are rather emphatic and their effects more or less transient. Oftentimes it is desirable, indeed much better, to maintain this passive hyperemia gently, continuously, and uniformly. The application of thin rubber tissue, as employed by Morris Longstreth, here serves a most satisfactory purpose. A part can be steadily influenced by wrapping the surface in rubber tissue. For example, the whole abdomen can be influenced uniformly and continuously. Thus are obtained the better effects of the now "taboo" poultice, which is indeed always—in proper cases—an excellent, reliable agency. A whole limb can be wrapped in tissue, inducing various desirable results, sometimes demonstrative of marvelous efficacy.

By means of a simple, yet especially good belt (also the device of Morris Longstreth) similar lasting and compelling effects are produced.[8] It is the

[8] This belt is the best device in my knowledge, and I have tried all the more promising ones. It is five inches wide, and is applied where alone it is safe, viz., about the massive structures of the hip bones,—never compressing the structures of the lumbar region, where compression would be distinctly hurtful. It is worn loose and low, seizing the relatively rigid and non-sensitive muscle-masses of the pelvic girdle. See article by author, "Rational Treatment of Splanchnoptosis," Medical Record, October 17, 1908.

only means I have found to lift satisfactorily the soft structures of the abdominal area, to free the hydrostatic mechanisms from compression, and hence from passive conditions, and to aid in the ebb and flow of fluids in waterlogged structures.

Conclusions.

1. In chronic disease the organism as a whole becomes exhausted through protracted, complex derangement; hence, reparative agencies are at a disadvantage as compared with the normal poise and efficiency of the organism when acute disease or injury arises.

2. Therefore, the pathology of chronic disease is something much more than that of acute states, involving many problems of morbid physiology and psychic disorder.

3. Remedial measures must be directed to the restitution of functional poise and should include all those rational measures capable of conserving and enhancing the autoprotective and autoregulative forces.

4. The basis of relief and cure is to be found along the line of palingenesis (development according to the primitive or original method); also of the overcoming of agencies which retard physiologic processes,—rehabilitation of all functional derangements, regulation of all contributory factors in vital action, so that full compensation shall be achieved of existing damagements.

5. The utmost drugs and medicine can do is to contribute to these desirable effects, however nearly they may approach to the rôle of "specifics," by overcoming disease entities, unlocking the doors for toxic wastes, and freeing the organism as a whole from disabilities present.

6. The measures on which, in the final count, we can chiefly depend are included under the term *personal hygiene:* (*a*) conservative personal hygiene; (*b*) constructive personal hygiene, and especially (*c*) reconstructive personal hygiene.

7. The possibilities of reconstructive personal hygiene lie in the direction of making available latent, undeveloped energies in any adult below the norm, from whatsoever cause; in systematically utilizing the inherent dynamics, and in raising the coefficient of efficiency.

8. The practical purpose of this paper is to call attention to the fact that much can be achieved by bringing into line the functional power of the organs and tissues so as to secure the completest transformation of kinetic into dynamic energy.

9. Special vigilance is urged upon clinicians in restoring tissue elasticity, mobility, normality in the hydrostatic mechanisms; in amplifying the functional powers of respiration, circulation, urination, the skin, etc., and in affording support for relaxed structures.

THE TREATMENT OF CHRONIC UNIVERSAL PERIHEPATITIS.

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CHRONIC universal perihepatitis, panserositis, polyserositis, multiple serositis, hyaloserositis, polyorrhomenitis, or pericarditic pseudocirrhosis of the liver, although recognized earlier, did not receive much attention until Pick published his article in 1896; since then it has been usually known as "Pick's pseudocirrhosis." The earliest recorded instance of this disease is probably that of Van Deen, in 1846. The *Zuckergussleber*—iced liver—described by Curschmann, in 1884, was already known to several writers, of whom presumably Rokitansky was the earliest, the record being 1842. This condition, when chiefly limited to the peritoneum, is generally, in Italy, known as Concato's disease, "phthisis of serous membranes." In France it is sometimes known as perivisceritis, or, better, as *symphyse péricardo-périhépatique.*

The anatomical conditions consist of a chronic adhesive pericarditis and enlarged liver, with ascites, although the necropsy may show pleuritis, peritonitis, perihepatitis, nutmeg atrophy of the liver, red atrophy of the liver, or hepatic cirrhosis in addition.

The symptoms are usually pain and fullness over the liver, and enlargement of the abdomen, due to ascites, but which is not accompanied by edema of the lower extremities. The jaundice is usually slight, but may be absent. The obliterative pericarditis usually escapes recognition, while the pleuritis and peritonitis are diagnosticated by their usual symptoms and signs, these presenting nothing peculiar in this particular disease. The ascites is, however, significant in its amount, rapid recurrence, and the apparently slight effect on the general health. This is in marked contrast to the ascites resulting from the usual forms of chronic hepatic cirrhosis. The large number of operations of paracentesis that may become necessary is notable—over 300 in the instance reported by Rumpf.

Although systematic authors do not, as a rule, include this condition in their works, yet when the disease is once recognized its identification is easy. Although my first patient had been under observation for some time previously, the disease was not recognized until the work of Pick was read. Two years later, when the second patient came for treatment, the diagnosis, in that instance, was readily made.

The cause of the disease has not, by any means, been definitely settled. Certain infectious diseases, as enteric fever, pertussis, syphilis, acute polyarthritis, and even malaria, have preceded the onset of this symptom-complex. The modern trend of pathological thought is to designate the tubercle bacillus

as the cause of chronic obliterative pericarditis, as well as of similar conditions in other serous membranes. Yet, it must be conceded that all instances of this disease are not of tuberculous origin, and some have been proved not to be so. On the other hand, the predominating terminal lesions may be tuberculous. As the course of events varies so much from the usual serous membrane tuberculosis, Cantu hazards the conjecture that it may be of especial, *e.g.*, of avian, origin.

The striking clinical feature of the disease is the ascites, which is present or may in the early stages be absent, with slight or marked pericardial and pleural changes. The symptoms resulting from the perihepatitis and peritonitis are striking; those from the pericarditis may be insignificant or even entirely unnoticeable. The ascites usually calls for intervention, and the fluid should be removed by paracentesis. When it recurs, it should again be removed, and this operation may be repeated indefinitely. The very fact that so many evacuations of the abdominal fluid have been carried out, and in the mean time the physical condition of the patient remains good, affords a valuable hint as to the correct diagnosis.

The means laid down as proper for the treatment of hepatic cirrhosis, viz., 1, diminution of the excessive connective tissue in the liver; 2, meeting the symptoms as they arise, and, 3, prevention of further connective-tissue change in the liver and consequent destruction of its parenchyma, are of comparatively little importance, because the lesions are largely perihepatic, or, at least, are not hepatic until very late in the disease. The methods of treating plastic pleuritis in vogue are applicable, as well as those adapted to the adhesive pericarditis, if, by chance, the latter should be recognized.

The difficulty which led to a careful study of the literature, and to a patient analysis of the symptoms which the earlier cases under observation had presented, was how to deal with the acute exacerbations which occurred from time to time. To one not recognizing the condition from which the patient was suffering, it would appear as if an acute infectious pneumonia, acute pleuritis, acute pericarditis, or even an acute peritonitis were imminent. In fact, the symptoms and the few physical signs, in addition to those always present, would lead to an incorrect diagnosis, if one's attention had not been called to the disease. A few or generally several days having elapsed, the error is readily detected.

After considerable study, and more experimentation, it was found that antipyrin salicylate, in 10-grain doses, given every two to four hours, would relieve the symptoms, and limit the duration of the exacerbations to a very few days or sometimes hours. Usually at the expiration of thirty hours the patient regains his normal condition.

Curiously enough, the ascites is not usually increased *pari passu* with the exacerbation of the symptoms.

While this condition is by no means frequent—the reported instances numbering but a few hundred—the likelihood of its existence when recurrent ascites without obvious cause or marked associated symptoms is present should be borne in mind. Attention should be given to its possible presence in a

given patient when the symptoms do not seem consistent. Failing a definitely known causation, although the course of the disease always suggests an infection, the treatment must be based upon experience, and that, indeed, is based upon the limited number of examples which are likely to be encountered. Finally, a correct diagnosis is desirable, permitting of a reliable prognosis, especially after abdominal paracentesis.

DISCUSSION.

Dr. Robert T. Morris, New York: I would like to hear some trend of thought, or discussion, or observation on the character of the infection. It seems to me that that is the best way we have to get very much more information in the next two years. We have a large group of infections, and, as Dr. Wilcox says, one side recommends trying one thing, and another trying another; so that we are very much in need of an elaborate analysis of the affections.

THE TREATMENT OF LEUKEMIA WITH THE MIXED TOXINS OF COLEY.

Abstract of Paper
By R. C. LARRABEE, M.D.,
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THE author stated that 5 cases had been previously reported, and he had now to report 13 additional ones: 9 of his own, 3 of Boldoff's, and 1 of Coley's. Under this treatment the general condition of the patients, some of whom had been treated with the X-ray without benefit, usually improved markedly, and in many instances there was a very marked diminution in the number of leucocytes. In other cases the leucocytes did not diminish, though the general condition improved. It was noticeable that, while the myelogenous cases were often benefited, the lymphatic cases showed no improvement. This mixed toxin treatment was to be regarded as merely palliative, not curative; but in many instances it added greatly to the patient's comfort, and no doubt prolonged life. It should not be forgotten, however, that it was a dangerous treatment, and ought, therefore, to be employed with the greatest caution.

DISCUSSION.

Dr. Satterthwaite: I have been conversant for a number of years with Dr. Coley's treatment, and I merely wish to add, in corroboration of what has been said, that the treatment should begin with small doses of the toxins; otherwise one may have most alarming results.

Dr. Morris: I think most of us would like an explanation, if we can have it, as to why the X-ray works so well in some cases and the toxins in others. I have noted that in some cases we get good results from the X-ray, while in others we get no response. We have to depend, however, upon the combined results of the X-ray and toxins in many of our cases.

Dr. Reynold Webb Wilcox, New York: At the last meeting of the Society I read a paper on the "Treatment of Leukemia by the Roentgen Ray." My personal observation with the X-ray work is that in the splenic forms we get temporary abeyance of symptoms; in other words we mitigate the symptoms very markedly in the majority of instances. In the myelogenous forms we do not get very definite results with the X-ray. On the other hand, it is very difficult to get in touch with the patients in order to determine the results of treatment, since, if they are helped, they are likely to disappear. So far as the Coley serum, in connection with the treatment of leukemia, is concerned, that, I think, becomes to a considerable extent a question of diagnosis, and there is, even where the appearance of the blood is perfectly characteristic, always a doubt as to the particular form of the disease—especially in the acute varieties. I hope Dr. Larrabee will bear me out as to the difficulties of diagnosis. Sometimes, in particular instances, there is a relapse, and this is likely to continue for a long time. That is my personal observation.

Dr. W. J. Boos, Boston: A recent article in the *Münchener medizinische Wochenschrift* deals with cases of myelogenous leukemia which were treated with dioxydiamidoarsenobenzol. The results in some of these were very good; one patient, a man who had been considered hopeless, went back to work and stayed at work for months. After a time the cases needed a repetition of the injection. The second injection produced as good results as the first.

Dr. Morris: I would like to ask Dr. Larrabee if there is any stage at which we should not begin treatment because of the hopelessness of the case. I saw a female patient who was supposed to have sarcoma of the spleen. She was really about to die, and I was asked to see the case more for the comfort of the family than anything else. I asked to have a blood examination, and Dr. Brooks from this made a diagnosis of myelogenous leukemia. Now the patient is out riding and enjoying fairly good health. The treatment by the X-ray was used, and it was this which brought her to the present condition.

Dr. Larrabee: In regard to the selection of cases of leukemia for treatment with the Coley toxins,—I know of no criterion which will guide us in determining which cases will be benefited by this method and which ones should have the X-ray. If the X-ray is available it should perhaps be tried first, as its effects are much better understood and it has been much more generally used. There are, however, many cases in which the X-ray cannot be used—*e.g.*, cases in the country and those in which the patient is confined to bed. Some cases will not improve with the X-ray, but will receive very much benefit from the toxins. So far as my experience goes, advanced cases are as likely to be benefited as early ones. We must emphasize the fact that neither the toxins nor the X-ray will *cure* leukemia. Both of these methods are simply means by which we can give the patient temporary relief. Nothing more can be expected from them at present. The use of the toxins is not unattended with danger. This fact should not prevent us from using them, though it should make us very cautious in increasing the dose. I believe that the internist, like the surgeon, must be prepared to take risks. I cannot altogether agree with what Dr. Wilcox has said as to the difficulty of diagnosis in leukemia. A well-marked case of leukemia is about as easy of diagnosis as anything can be. Doubtful leukemias are very rare. Moreover, in the blood-smear we can preserve a pathological specimen which can be used to verify the diagnosis at any time. I have not used dioxydiamidoarsenobenzol in leukemia at all, though I am aware that favorable results have been reported. It is too early for us to judge of anything in regard to their permanence. Personally I am skeptical, just as I am in regard to the permanence of the results of this remedy in pernicious anemia.

Dr. Morris: Can it be said that it makes no difference about the stage of the case, and can you use the toxins as long as you get any benefit?

Dr. Wilcox: I think that I failed to express myself clearly. There is a difficulty in determining the forms of leukemia and there is a difference of opinion as to what should be the characteristics of one variety as contrasted with the other. The other difficulty is what Dr. Morris has expressed. There is a difficulty in many acute instances in determining the type of leukemia: in differentiating the lymphatic from the myelogenous form.

Dr. Larrabee: I recognize the difficulty. While sometimes it is most easy, sometimes it is very hard to make the distinction. I believe that some cases said to be acute lymphatic leukemias are really myelogenous, as the very young myelocytes, or "myeloblasts," very closely resemble lymphocytes.

HYPOADRENIA AS A CAUSE OF DEATH IN INFECTIONS AND ITS TREATMENT.

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Not many years have elapsed since sneers, not to say ridicule, met the efforts of those who laid stress on the clinical importance of the ductless glands. Fortunately the tide has turned, and with such vigor that the time is fast approaching when to ignore these organs, even in the course of routine practice, will mean a willful compromise of the issue in a large number of serious diseases. Especially does this apply to the class of cases to which I am about to refer.

In the course of many infections, especially among children, there are two very fruitful causes of death that are practically unrecognized, and the identification of which, on the other hand, yields a rich harvest of recoveries. Both include as lethal factor arrest of the functions of the adrenals, which, from my viewpoint at least, entails arrest of pulmonary and tissue respiration. In the short space of time available it is possible to refer to but one of these types: that which I have ventured to designate "terminal hypoadrenia." By terminal hypoadrenia I mean that form of adrenal insufficiency which occurs late in the course of a febrile disease, as a result of exhausting secretory activity, probably aggravated by temporary local lesions to which the adrenals are subjected during the early or febrile period of the disease.

The adrenals being admittedly concerned in the protection of the organism during infections and intoxications,—by contributing an excess of their secretion during the febrile stage of the disease (sometimes considerably prolonged),—it follows that, after this stage is over, the adrenals should lapse into a condition of temporary greater or less insufficiency through fatigue or exhaustion. That other organs concerned in the immunizing process are influenced in the same way must doubtless be the case, but the fact remains that it is the symptomatology of hypoadrenia which is uppermost.

In lobar pneumonia and bronchopneumonia, for instance, resolution may be considerably delayed; convalescence likewise. There is, late in the case, extreme adynamia and a low blood-pressure; the temperature is below normal, the pulse is weak and more or less rapid, and death from heart-failure is not infrequent. In typhoid fever, hypoadrenia is commonly observed. The disease assumes what is now known as the cardiac type, with, late in the case, extreme prostration; a rapid, weak, and sometimes irregular pulse, hypothermia, and a marked tendency to vertigo, fainting, and cardiac failure.

Sicard[1] reported the case of a young woman in whom the foregoing symptoms appeared on the ninth day of a bronchopneumonia. Extreme muscular weakness, marked hypothermia and low blood-pressure, diarrhea, and

Sergent's white line, which denotes marked adrenal insufficiency, were present. On the fifteenth day the blood-pressure fell to 70 or 80 mm. Hg., and death followed three days later. At the autopsy the adrenals were found hemorrhagic. This suggests that adrenal lesions may be present in all such cases. Yet, Ribadeau-Dumas and Bing[2] have witnessed the same symptoms in cases of measles which recovered, while Bossuet[3] refers to 8 cases in various febrile disorders in which typical symptoms of adrenal insufficiency, asthenia, low blood-pressure, etc., developed suddenly and disappeared spontaneously, aided perhaps by adrenal extract which had been administered.

As stated recently by Morichau-Beauchant,[4] the adrenals seem to show a special susceptibility to certain infections. Diphtheria easily leads them all in this connection. So seriously do the organs suffer in these cases that Sévestre and Marfan have termed the type "secondary syndrome of malignant diphtheria." Hutinel ascribes the fulminating cases of scarlatina to this cause. Tetanus, erysipelas, mumps, certain forms of tonsillitis, and certain streptococcic infections are occasionally witnessed which also present the typical syndrome of hypoadrenia. Goldzicher[5] was led by his researches to conclude that in the various forms of septicemia the appearance of lower blood-pressure was to be ascribed to insufficiency of the adrenals.

Pathogenesis and Symptomatology.—If at the end of an infectious disease the case, instead of proceeding to convalescence, remains in a condition of asthenia, with low blood-pressure and temperature, there is good ground for the conclusion that terminal hypoadrenia has occurred. Exhaustion of the adrenals during the acute process having inhibited their secretory activity, the above symptoms result from inadequate oxidation of, and metabolic activity in, the tissues. Sergent's white line may be obtained in the majority of these cases. It is elicited by gently rubbing the finger in a narrow line over any part of the abdomen. After a short period the area becomes whitish, and remains so a short time. The patient complains of chilliness; the surface is pale owing to the poverty of the blood in cellular elements and hemoglobin, and to recession of the blood-mass from the surface to the deeper vascular trunks. The vascular tension being low, the pulse is rapid and the heart-beat weak. Anorexia due to deficient metabolism and diminished food intake, nausea, the result of relaxation of the gastric muscular coat, and diarrhea due to a similar condition of the muscular coat of the (already passively engorged) intestine, more or less frequent fainting spells,—are all concomitant symptoms that may be witnessed in such cases, which are always greatly exposed to relapse or to sudden death from heart-failure.

Complications of various kinds may occur, the immunizing processes being greatly weakened through the deficiency of adrenal secretion, one of their important factors. Septic infection, abscesses, bone lesions, tuberculosis of a rapid type, and other infections may develop more or less rapidly. Disorders of nutrition, cholelithiasis, and occasionally Addison's disease may also appear. In acute pulmonary infections, pneumonia, for example, structures in the neighborhood of the focus of infection, the pleura, the heart, etc., inadequately protected by the blood and its phagocytic cells, become the prey of specific

bacteria. Briefly, the body is rendered vulnerable to the attacks of almost any pathogenic organism.

Pathology.—In the special type in question no adrenal lesion may be discernible. In the majority of instances, however, the organs are enlarged and congested, and may show here and there a limited hemorrhagic area. Their appearance suggests not only the functional torpor incident upon functional exhaustion, but the presence of a *passive* congestion resulting from loss of resiliency of their sinusoidal vessels, the circulation through them being thus impeded. Occasionally they are the seat of suppuration,—a complication likely to be observed when the causative disease is, or includes, a streptococcic infection, pneumonia, or meningitis.

The pathological picture of the more severe form of adrenal complication, viz., intercurrent hypoadrenia, shows far more distinct lesions of the adrenal parenchyma. Hence the typical lethal phenomena that attend many of these cases.

Treatment.—In this particular disturbance, opotherapy, or rather the use of adrenal gland, or of pituitary body,—which acts very similarly, but with less violence and more lasting effects,—sometimes gives surprising results. The adrenal product—which from my viewpoint is also the main active agent in the neural lobe of the pituitary, as shown by the chromaffin test—insures precisely what the body needs, viz., the resumption of all oxidation processes, and also, therefore, general metabolism and nutrition. This in turn causes a rise of blood-pressure, which causes the blood to circulate normally in all organs, including the skin, and in the adrenals themselves. Indirect effects are also obtained: the action of the adrenal principle on the heart increases the contractile power of this organ, and, since it is thus rendered capable of projecting the blood with greater vigor through the lungs, oxygenation of the blood becomes more perfect. Recovery is also materially aided by the rise of blood-pressure which the adrenal product insures, and which causes arterial blood to be driven from the splanchnic area toward the peripheral organs, including the lungs and the brain. From these features alone, considerable benefit is derived. If we recall, moreover, the participation of the adrenal secretion (which the adrenal preparation administered represents) in the immunizing process, we have the added factors of ridding the blood of any intermediate—and, therefore, toxic—wastes, bacterial toxins, etc., it may contain, and of increasing phagocytic activity, thus antagonizing efficiently any pathogenic organism that may remain to compromise the issue. Thus explained, we can understand the phrase "little short of marvelous" applied to the results obtained by some clinicians. We can also understand the marked reduction in the mortality obtained by Hoddick[6] in cases of peritonitis following appendicitis accompanied by uncontrollable decline of the blood-pressure, cyanosis, and other evidences of collapse, and also in puerperal toxemias, by the slow intravenous use of adrenalin in saline solution. Hoddick ascribes the lowering of the blood-pressure to paralysis of the vasomotor center; but as the toxemia is the cause of this condition, an agent capable of counteracting both cause and effect is necessary. This is met by the adrenal principle. Josué,[7] in typhoid fever, likewise relieved threatening

symptoms by injecting 15 minims (1 c.c.) of the adrenal active principle (1:1000 sol.) in ½ to 1 pint (250 to 500 c.c.) of physiological saline solution subcutaneously. The influence of the saline solution in these cases must not be overlooked, however. Eight years ago, I urged that death was often due, in infectious and septic diseases, to the fact that the osmotic properties of the blood became deficient, and advised the use of saline solution *from the onset* of the disease. The reduction in the mortality of pneumonia in the practice of men who have carried out this suggestion has demonstrated its value. Netter[8] has used much larger doses of the adrenal active principle with profit. Marran and Darré[9] found it of great value in the collapse of diphtheria with marked asthenia, low blood-pressure, and subnormal temperature. Moizard[10] recommends adrenal organotherapy as soon as asthenia and low blood-pressure occur in any infection. He gives daily two fresh adrenals from the sheep, finely divided and mixed with powdered sugar, or administers the active principle, 10 to 20 drops daily divided in 5 or 6 doses. Kirchheim[11] has found large doses —10 to 24 minims—safe hypodermically in the collapse of pneumonia, diphtheria, and scarlet fever. Letulle has found the principle of great value in the latter disease. The better plan, from my viewpoint, is to inject it with saline solution (at 108° F.) intravenously, the needle of the syringe containing the principle being inserted into the rubber tube of the saline solution apparatus.

These measures are only indicated in emergency cases, however. In the average case the *glandulæ suprarenales siccæ* of the U. S. P., administered by the mouth, are fully as effective, if a good preparation is obtained, as soon as asthenia and low blood-pressure appear. The powder in 3-grain (0.2 Gm.) doses three times daily in capsules, gradually increased until 5 grains are given at each dose, usually suffices. When the cardiac adynamia disappears, a small dose of thyroid, the desiccated gland, ½ grain (0.03 Gm.); strychnine, 1/60 grain (0.001 Gm.), and Blaud's pill, 1 grain (0.06 Gm.), added to each capsule greatly hasten convalescence. The iron and the adrenal product serve jointly to build up the hemoglobin molecule, a slow process when left to itself.

For our knowledge of the action and use of pituitary extracts in infectious diseases we are mainly indebted to L. Rénon and Delille,[12] who began their use in 1907. In a recent work in which the clinical observations of both observers are recorded Delille,[13] referring to grave cases of typhoid fever, states that they showed "arterial hypotension, irregularity of the pulse (especially the grave forms), oliguria, insomnia; while convalescents showed asthenia, hypotension, or at least 'effort hypotension' (Oddo and M. Achard), paroxysmal or continuous tachycardia"—all, we have seen, symptoms of hypoadrenia or adrenal insufficiency. They found 1½ grains of pituitary extract (of both lobes), at noon daily, extremely efficient; it counteracted at once the depressed arterial tension, produced diuresis, overcame insomnia, and greatly improved the general condition. Similar effects were observed in diphtheria and erysipelas. The results in pneumonia do not appear to me to warrant the use of any adrenal or pituitary preparations early in the case,—the first few days of the disease, when the blood-pressure and the fever are

high. They should be used *only when a low blood-pressure and other symptoms of hypoadrenia are present.* The results reported by Delille strengthen this opinion. In advanced tuberculosis no beneficial effect was observed.

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MALIGNANT ENDOCARDITIS IN NEW YORK CITY: A CLINICAL STUDY.

Abstract of Paper
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AMONG pathologists this disease is believed to be a simple endocarditis which has become infected with poisonous germs. It then assumes so grave a type that the word malignant is an apt prefix. It is so rare an affection that no one person can have had much personal experience with it, nor can anyone discuss it intelligently without having studied a large number of cases at first hand. I have had the unusual opportunity of studying 100 cases in the record books of some New York hospitals, and the chief object of this paper is to present a brief analysis of what the examination has yielded.

In this disease there is a poisoning by implantation in the inflammatory deposit of the valves. The poisoned emboli, together with aggregations of bacteria, are carried forward by the blood-current into the greater circulation, infecting the entire system. The cases analyzed were sometimes examples of mixed infection. Thus, in the 100 cases, of which 33 showed specific germs in the blood or elsewhere, streptococci were found alone in 18; staphylococci occurred conjointly with these in 1; staphylococci occurred alone in 5; pneumococci were associated with them in 2; pneumococci occurred alone in 6, and the gonococcus in 1. It is clear, therefore, that the predominating germs were of the pus-producing varieties. The statistics of the 100 cases indicate that malignant endocarditis is largely a disease of early middle life, occurring with greatest frequency between the ages of 30 and 40 years, almost never under 4, and but seldom before 14 or after 60. With very rare exceptions, the disease is accompanied with fever. In these cases high temperature was the rule. In the larger number of instances it reached 104° F.; in 73 per cent. it varied between 103° and 106°; in 14 per cent. it touched or passed 106°, and in 2 per cent. it exceeded 107°. Petechiæ were noted in 19 per cent., hemorrhages in 5 per cent., and implication of the spleen in 8 per cent. Headache and diarrhea were frequent. Rheumatism was a concomitant in 37 per cent., pneumonia in 6 per cent., tuberculosis in 5 per cent., pleurisy in 3 per cent., syphilis in 3 per cent., gonorrhea in 2 per cent., acute and subacute nephritis in 2 per cent., and cerebrospinal meningitis, mammary abscess, suppurative arthritis, colitis, chancre with suppurative buboes, chronic appendicitis, gangrene of foot, and miscarriage each in 1 per cent. The leucocyte count varied from 6650 to 36,000; it exceeded 20,000 in only five instances. Sometimes the diagnosis presents great difficulties, and has to be made by exclusion, for often the symptoms are variable and indefinite and lead to the confounding of the disease with tuberculosis, purpura, typhoid or malarial fever. It is here that a blood-culture comes to our aid, though we cannot depend absolutely on culture methods. They fail in a certain number of cases, and the germs may not be

recovered during life. Inasmuch as the pathological diagnosis may be inconclusive, we must learn not to wait for it, but make independently, if we can, a clinical diagnosis. Basing our prognosis on these 100 cases, we may conclude that 85 per cent. die, that 10 per cent. improve for a time, and that 5 per cent. improve to such a degree that the result may be called recovery in so far as the malignant nature of the disease is concerned. The number of weeks spent by patients in the hospital before the fatal issue varied from one to thirteen, the majority succumbing before the end of the fifth week. Antigonococcal serum was used in 1 case, other sera in 3, and vaccines in 5; but in no instance was there recovery under these forms of treatment. In any event, the indications are for rest, good and abundant food, the liberation of pus when practicable, and the use of quinine sulphate, and perhaps iodine, internally, and supporting treatment generally.

DISCUSSION.

Dr. Stewart: One of the most important parts of Dr. Satterthwaite's paper is that in which he refers to bacterial therapy. Three factors must always be considered in relation to the use of bacterins, namely: the nature of the infecting germ or germs, the character of the bacterin or serum employed, and the amount and interspacing of doses. First, in regard to the nature of the infection. We are beginning more and more to realize that many cases of disease caused by pathogenic bacteria are mixed infections. It is not enough to say, use antistreptococcic serum for streptococcic infection. Other pathogenic germs may be present. In a recent case in which I advised the use of this serum because examination of the spinal fluid apparently demonstrated the cause of the meningitis present to be a streptococcic infection, the post-mortem revealed the presence of the tubercle bacillus. The patient had improved under the antistreptococcic serum, and no streptococci were found after death, but the primary infection was evidently tuberculous.

Second, the character of the serum or bacterin. In the treatment of streptococcic infections with antistreptococcic serum it is always necessary to use a polyvalent serum. The same statement applies to streptobacterin. There are many varieties or strains of streptococci, and we should use a serum or bacterin prepared from strains of streptococci identical with those causing the pathological condition. This is an argument in favor of autogenous vaccines; but the use of autogenous vaccines is not always practicable, and autogenous sera do not exist, for obvious reasons. Polyvalent, as referred to a bacterin, for example, means that the suspension contains bacteria of the same species, but from many different sources. The bacteria used for its preparation should not only all be streptococci, but be obtained from a great variety of human infections. The same principle applies to the preparation of a serum. Manifestly better results will be secured from a polyvalent antistreptococcic serum than from one not polyvalent. In reporting the results of bacterial therapy this should be borne in mind. Mixed bacterins should be employed in mixed infections, unless an autogenous vaccine is used. A mixed bacterin is one which contains the various bacterial species generally present in a mixed infection. A mixed gonorrheal infection may show the presence of no less than seven kinds of bacteria.

Third, in regard to the amount and interspacing of doses. Dr. Barton Cook Hirst, who has had much experience in the use of a certain brand of antistreptococcic serum, tells me that it is essential to give at least 100 c.c. of it during twenty-four hours in order to obtain the brilliant results frequently secured with it in his service at the hospital of the University of Pennsylvania. I used the expression "a certain brand" because he also called my attention to the great discrepancy observed in reports of results obtained in the use of different brands of serum. This illustrates why there

should be common standards for sera and bacterins. Clinical control for the guidance of dosage is more practical than the opsonic index, and this can be learned only by experience. The amount of bacterin to be given as an initial dose is not as important as it is to learn to tell how much to give altogether and how frequently to repeat the dose.

Finally, I desire to express the satisfaction I have derived from Dr. Satterthwaite's admirable paper, as it shows that he appreciates the necessity of standardizing materia medica products if they are to be made in fact instruments of precision. And I hope the time may speedily come when the American Therapeutic Society may work in co-operation with the American Pharmaceutical Association in fixing standards for the nomenclature, character, quality, and strength of the new materia medica products constantly presented to the profession.

THE NUTRITION LABORATORY OF THE CARNEGIE INSTITUTION OF WASHINGTON AT BOSTON, MASS.*

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The Nutrition Laboratory is designed primarily for studying problems in metabolism, with special reference to the gaseous exchanges and to the energy transformations in the human body.

A large laboratory on the ground floor is constructed for calorimetric investigations, and is provided with arrangements for securing even temperature and humidity during the time the experiments are in progress. Three respiration calorimeters for use with men are completely equipped and in running order; a fourth is in process of construction, and a fifth is being designed. In these chambers the subject is placed in an air-tight inclosed volume of air, which is constantly purified by being withdrawn from the chamber, passed through purifying vessels containing sulphuric acid, to absorb water, and soda-lime, to absorb carbon dioxide, and then returned to the chamber, the deficiency in oxygen consumed being made up by admitting oxygen automatically from a cylinder of the highly compressed gas. By noting the loss in weight of the oxygen cylinder, the amount of oxygen absorbed in a given period is found. The increase in weight of the water-absorbing vessels gives the water vaporized, and the increase in weight of the soda-lime containers gives the carbon dioxide produced.

The calorimetric features of the apparatus are based upon the refrigerator type of construction, *i.e.*, with a number of insulating walls. The heat given off by the body of the man is absorbed by a current of cold water passing through a pipe inside the chamber, the rise in temperature of the water as it passes through being noted and the amount of water, these two giving the required data for computing the heat given off. Special adiabatic arrangements for controlling the temperature of the chamber, and thus prevent loss of heat from the walls, make the heat measurements, by means of the current of water and the temperature rise, absolute.

In addition to the respiration calorimeters, many forms of apparatus for studying the respiratory gases are in use, particularly a new form in which the subject breathes through a nosepiece or mouthpiece into a ventilating current of air and the carbon dioxide excreted and the oxygen consumed thereby accurately measured. The experiments with this type of apparatus may be as short as fifteen minutes, and the apparatus is especially adapted for use in hospitals or physiological laboratories. The building is thoroughly well equipped with a machine shop, and all possible construction can be carried out inside the building.

* Abstract of remarks demonstrating the Laboratory to the members of the American Therapeutic Society, May 11, 1911.

An apparatus for determining the heat of combustion of foods, feces, and urine, a large number of forms of gas analysis apparatus of the highest and most improved type, a dog-respiration chamber for studying the respiratory gases of dogs, and several well-equipped chemical laboratories complete the equipment.

The final results involve a large amount of computation, and a computing staff is constantly employed. The researches are made public either in the standard accredited scientific journals or the larger reports, which partake of a monograph nature and are published by the Carnegie Institution of Washington.